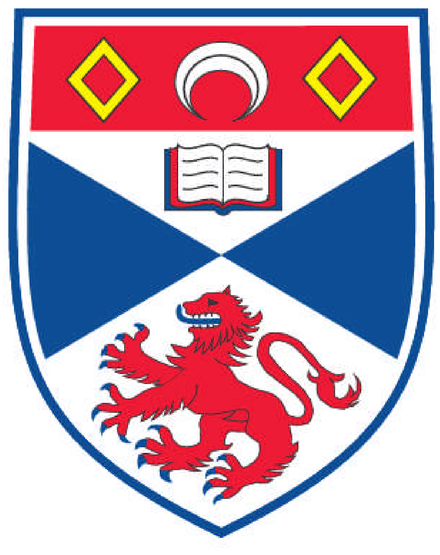
1,2-BIS-(DITERTBUTYLPHOSPHINOMETHYL)BENZENE IN CATALYSIS

Cristina Jiménez

A Thesis Submitted for the Degree of PhD
at the
University of St. Andrews



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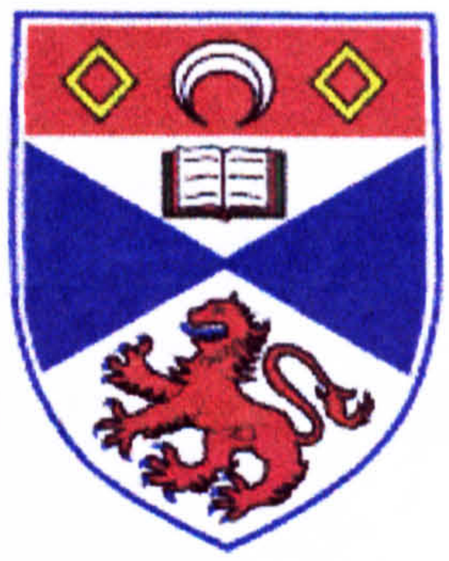
1,2-bis-(ditertbutylphosphinomethyl)benzene in Catalysis



A thesis presented by

Cristina Jiménez

to the

University of St Andrews

In application for

THE DEGREE OF DOCTOR OF PHILOSOPHY

St Andrews September 2004

DECLARATION

I, Cristina Jimenez, hereby certify that this thesis, which is approximately 47000 words in length, has been written by me, that it is the record of work carried out by me and that it has not been submitted in any previous application for a higher degree.

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Abstract

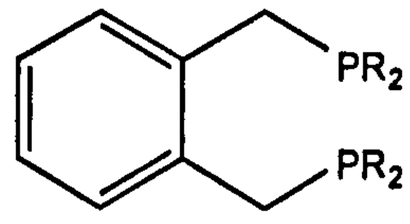
Different diphosphine ligands having the structure shown below have been studied for carbonylation and hydroformylation reactions.

Depending on the substituent on the phosphorus atoms the electronic and steric properties can be tuned to direct the reaction towards the desired products.

Palladium methoxycarbonylation of a large variety of unsaturated compounds has been attempted under very different conditions. The outcome of these reactions was the achievement of the linear products with a selectivity higher than 99.5 % under mild conditions of pressure and temperature.

Chloroaromatic compounds have also been employed as substrates in methoxycarbonylation reactions. Unexpected results were observed since carbonylation was possible only when a strong electron withdrawing group was present. The origin of the many side products from these reactions has been elucidated.

Rhodium hydroformylation was not as successful as palladium methoxycarbonylation, since relatively severe conditions had to be used to get good rates and good selectivity. In no case were there as good as those obtained in the carbonylation reactions. However, unusual factors, such as the presence of chlorine in the reaction media, have been found to influence either the conversion or the selectivity.



R= t-Bu
R= i-Bu
R= Ph
R= Cyclopentyl

Abbreviations

AA	allyl alcohol
acac	η^2-acetylacetone.
b	Branched.
^{t}Bu	*tert*-Butyl.
^{t}BuOH	*tert*-butanol.
CATS	Catalytic Evaluation and Optimisation Service.
cod	Cyclooctadiene.
Conv	Conversion
cot	Cyclooctene
dba	*trans,trans*-dibenzylideneacetone
DCM	Dichloromethane
DHPE	1,2-bis(diphosphino)ethane
DHPP	1,2-bis(diphosphino)propane
DIOP	(-)-2,3-O-Isopropylidene-2,3-dihydroxy-
	1,4-bis(diphenylphosphino)butane.
DIPPMB	1,2-bis(diisopropylphosphinomethyl)benzene
DME	Dimethoxyethane
DMA	N,N'-dimethylacetamide
DMF	N,N'-dimethylformamide

DPPB	1,2-bis(diphenylphosphino)butane.
DPPE	1,2-bis(diphenylphosphino)ethane.
DPPF	1,1'-bis(diphenylphosphino)ferrocene.
DPPP	1,2-bis(diphenylphosphino)propane.
DPPMB	1,2-bis(diphenylphosphinomethyl)benzene
DCyPMB	1,2-bis(dicyclopentylphosphinomethyl)benzene
DIBPMB	1,2-bis(diisobutylphosphinomethyl)benzene
DTBPMB	1,2-bis(ditertiarybutylphosphinomethyl)benzene
DTBPP	1,2-bis(ditertiarybutylphosphino)propane
DTBPE	1,2-bis(ditertiarybutylphosphino)ethane
DIPPP	1,2-bis(diisopropylphosphino)propane
DPPOMF	1,1'-bis(diphenylphosphino)octamethylferrocene.
EtOH	Ethanol
Ethgly	Ethyleneglycol
GC	Gas chromatography.
GCMS	Gas chromatography mass spectrometry.
HB	4-hydroxybutanal
HF	2-hydroxyfuranol
HMP	3-hydroxy-2-methylpropanol
Isom	Isomerisation
K^{t}BuO	Potassium *tert*-butoxide

KOH	Potassium hydroxide
l	Linear.
NaOAc	Sodium acetate
MeOH	Methanol
MP, MEP	Methyl propanoate
MSA	Methane sulphonic acid
NEt_3	Triethyl amine.
OAc	Acetate.
OctMiMTfN	Octylmethylimidazolium triflamide
P	Pressure
P^iBu_3	Triisobutyl phosphine.
P^tBu_3	Tritertiarybutyl phosphine.
PCy_3	Tricyclohexyl phosphine
POSS	polioctavinylsilsesquioxane
PPh_3	Triphenyl phosphine
P^iPr_3	Triisopropyl phosphine.
^iPr	*iso*-Propyl.
RT	Room temperature
Selec, S	Selectivity
S ald	Selectivity to aldehydes
S linear	Selectivity to linear aldehyde

T	Temperature
t	Time
THF	Tetrahydrofuran.
TFA	Trifluoroacetic acis
TFE	Trifluoroethanol
TPP	Triphenylphosphine.
Tppts	Tri(m-sulfophenyl)phosphine solution
Triethgly	Triethyleneglycol
TsOH	p-toluenesulphonic acid
TfOH	Triflic acid

7. Experimental

Chapter 1:

INTRODUCTION

1.1. Introduction.

Transition metal complexes have been used in industry as catalysts for the synthesis of organic compounds since 1910. However, it was at the end of the 40's when they started to provide an important area for study. Scientists like Roelen, Wacker, Reppe, Wilkinson, Ziegler and Natta built the basis of the homogeneous catalysis we know today.

Many of the processes carried out by industry involve a transition metal based catalyst at some stage. The most important advantage of homogeneous catalysis over heterogeneous is the production of pure compounds in high yields under mild conditions. Working in the liquid phase not only makes the temperature and the mixture of products more controllable, but it also makes possible to define exactly the active species in the catalytic cycle, whereas none of these can be done when working on the surface of a solid. Therefore, mechanisms of different reactions have been studied, so that processes could be optimised and new catalysts have been developed.

Some important industrial processes catalysed by organometallic complexes and not requiring gases are isomerisation, polymerisation or alkene methathesis (*Figure 1- 1*):[1]

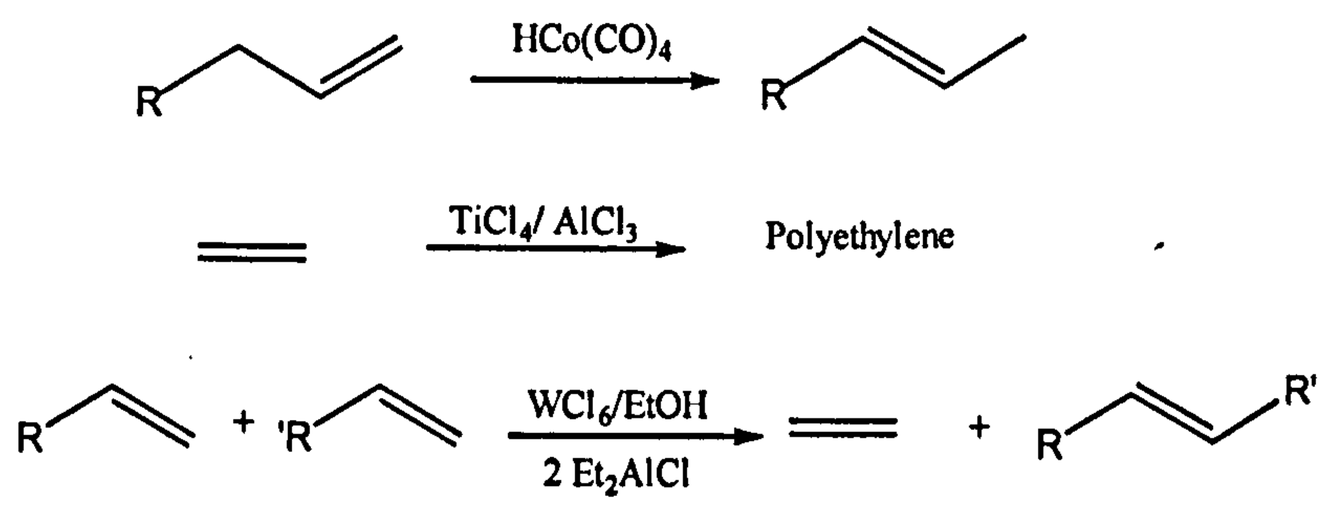


Figure 1- 1: Non gas requiring processes.

However, most of the important industrial processes involve gases at some stage. For instance, in the Wacker process organic, intermediates such as acetaldehyde, vinyl chloride or vinyl acetate are produced from ethene and O_2 in the presence of $PdCl_2$ and $CuCl_2$ as cocatalyst (*Figure 1- 2*).[2]

$$C_2H_4 + PdCl_2 + H_2O \longrightarrow CH_3CHO + Pd + 2\,HCl$$
$$Pd + 2\,CuCl_2 \longrightarrow PdCl_2 + 2\,CuCl$$
$$2\,CuCl + 2\,HCl + \tfrac{1}{2}\,O_2 \longrightarrow 2\,CuCl_2 + H_2O$$

$$C_2H_4 + \tfrac{1}{2}\,O_2 \longrightarrow CH_3CHO$$

Figure 1- 2: Wacker process.

Driven by the increasing need to produce oxygenated compounds from cheap hydrocarbons, Roelen, in 1930, developed the hydroformylation reaction (the addition of a formyl group to a double bond), which became the most commercially important reaction catalysed by transition metal complexes in homogeneous conditions (*Figure 1- 3*).[3]

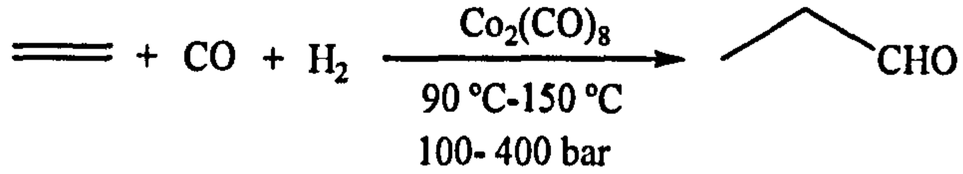


Figure 1- 3: Ethene hydroformylation.

Depending on the reaction conditions carbon monoxide can be hydrogenated to give organic products like ethene, 1,2-ethanediol, ethanol or methanol. This type of process requires high pressures and temperatures, 500-3400 bar and 210 °C-250 °C. This way of making methanol is not especially attractive, since heterogeneous catalysts based on copper can produce it in a fast and clean reaction using milder conditions of pressure and temperature. Acetic acid has been made by methanol carbonylation for over 30 years (Monsanto process) and has been deeply studied since an active catalyst at low pressure was discovered. This product is mostly used for vinyl acetate, in paints, as a co-adherent. The direct

production of acetic anhydride from methanol is also of great industrial importance.[4]

Carboxylic acids and esters can also be produced from carbonylation of alkenes in the presence of H_2O or ROH (*Figure 1- 4*):

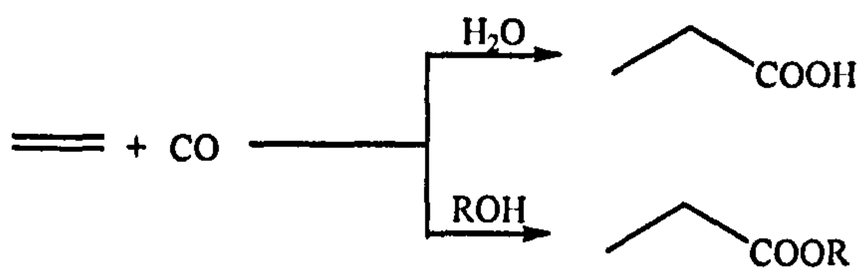


Figure 1- 4: Carbonylation of alkenes.

Both hydroformylation and carbonylation have been greatly improved since the 60's, when catalysts based on nickel, cobalt and iron carbonyls were replaced by phosphine based rhodium and palladium catalysts, which turned out to be more active and selective under milder conditions. Wilkinson discovered that triarylphosphine modified rhodium complexes were extremely active hydroformylation catalysts.[6] The most famous catalyst precursor is $[RhH(PPh_3)_3CO]$, which forms $[RhH(PPh_3)_2(CO)_2]$ under carbon monoxide and hydrogen, and $[RhH(PPh_3)_2(CO)]$ as the active species during the hydroformylation reaction. A high triphenylphosphine to rhodium ratio is required to prevent the formation of the less active and selective (towards the desired linear aldehyde product) monophosphine complex, $[RhH(PPh_3)(CO)_2]$, during the reaction. In 1969, Pruett and Smith reported that phosphite ligands, both aryl and alkyl, were effective ligands for rhodium catalysed hydroformylation of 1-octene and methylacrylate.[7] The use of diphosphines as ligands in the hydroformylation reaction has recently become a topic of much interest. This has been due to reports of greatly improved l:b ratios over those obtained when using monophosphines as ligands.

Pittmann suggested, in 1978, that the use of *cis*-chelating diphosphines as ligands in the rhodium catalysed hydroformylation could lead to high activity and selectivity towards the linear product.[8] This is understood considering that chelating ligands favour the species $[RhH(CO)_2(PR_3)_2]$ over $[RhH(CO)_3(PR_3)]$ and it was known that the former gives better selectivity towards the linear isomer.[9]

1.1.1. Ligand parameters

The effects of the phosphorus ligands on reactions had been explained only in terms of electronic properties until Tolman studied their steric effects. Since then it has become apparent that steric effects are as important as electronic effects determining the activity, stability and selectivity of the complex catalysts. Tolman defined the concept of cone angle, θ, for monophosphines as the apex angle of a cylindrical cone, centred at 2.28 Å from the centre of the P atom, which touches the outermost atoms of the phosphine.[5a] Since the importance of diphosphine has been growing since the 1970s it was necessary to extend the definition to include them for electronic and steric mapping. Other parameters have been reported, such as the solid angle[5b,5c] and pocket angle.[5d] However, the simplest way to approach the steric effects of bidentate ligands is to consider the bite angle.[10] The four substituents at the two phosphorous atoms of a diphosphine and the length of the bridge determine the steric properties. When the distance between the two phosphorus atoms is two carbon atoms, five-membered rings, which are the most stable, are formed. However, this is only true when the geometry of the complex is octahedral or square-planar, since the "metal-preferred" P-M-P angle is ~90°.

For tetrahedral complexes this angle is ~109° and bisequatorial coordination in a trigonal bipyramidal requires an angle of 120°.

In a catalytic reaction different intermediates are involved, so different coordination modes may be required. The preference for a certain angle might affect the stability of the initial, transition or final states of the intermediates as well as the flexibility.

Casey and Whiteker designed a way of predicting the natural preferred P-M-P angle (i.e. that preferred by the ligand ignoring geometry preferences of the metal).[10] They defined the concept of bite angle, β_n, and flexibility range for diphosphine ligands. Bite angles are estimated by using computer programs. The "flexibility range" is defined as the range of bite angles a ligand can adopt if conformations with energies slightly above that of the minimised structure are considered. It has been calculated and defined as the range of bite angles accessible within 3 kcal mol^{-1} of the minimum energy.

1.1.2. 1,2-bis(di-tertbutylphosphinomethyl)benzene as ligand

Ethene carbonylation

Palladium catalysts for alkoxycarbonylation of alkenes show a strong dependence on the nature of the phosphine, since monodentate phosphines give high selectively to ester and bidentate phosphines usually give high molecular weight polymers.[18, 19]

The catalyst system prepared from $[Pd(OAc)_2]$-PPh_3 and an acid of a weakly or non-coordinating anion in methanol produced methyl propanoate whilst using bidentate ligands, such as $Ph_2P(CH_2)_3PPh_2$, polyketones were the only products. This dramatic difference displayed by monophosphines and diphosphine was rationalised by the cis-*trans* isomerisation exhibited by the former. Phosphine

ligands in a *trans* orientation to one another avoid the unfavourable occurrence of a Pd-P bond *trans* to a Pd-C bond and reduce the steric interactions of the bulky PPh_3 ligands. As *cis-trans* isomerisation is possible for these intermediates, as soon as the acyl complex is formed, the two PPh_3 ligands rearrange from being mutually cis to *trans*. Thus, as the vacant coordination site is *trans* to the acyl chain, further chain growth is inhibited. The acyl intermediate can then be terminated by methanolysis to yield methyl propanoate (*Figure 1- 5*).

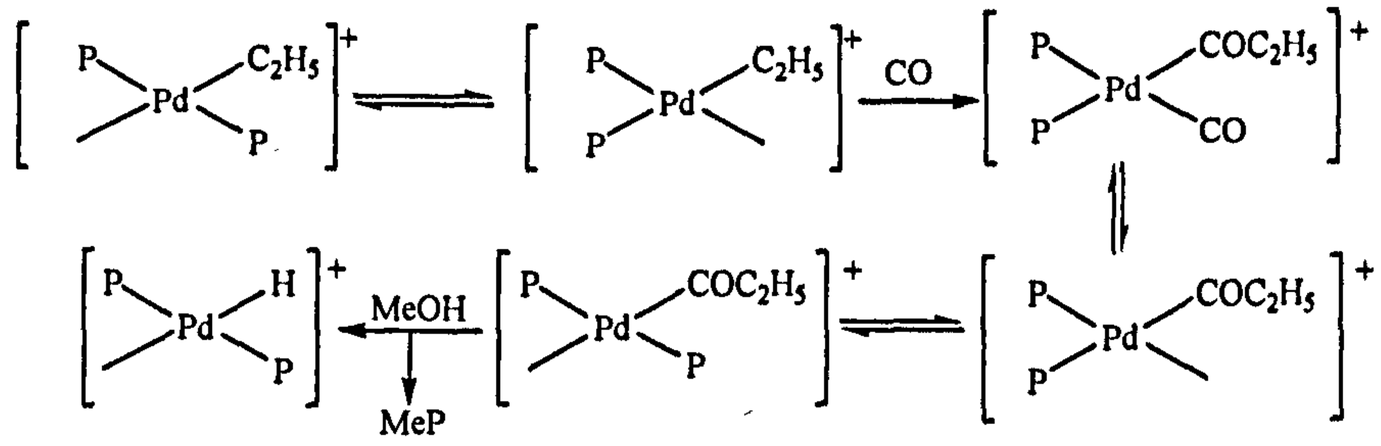


Figure 1- 5: Formation of methyl propanote.

Because of the impossibility of geometric isomerisation for cis-chelated diphosphine ligands, such as dppp, cis orientation of the vacant coordination site and the growing chain is imposed, favouring multiple insertion and therefore the production of polyketones (*Figure 1- 6*).

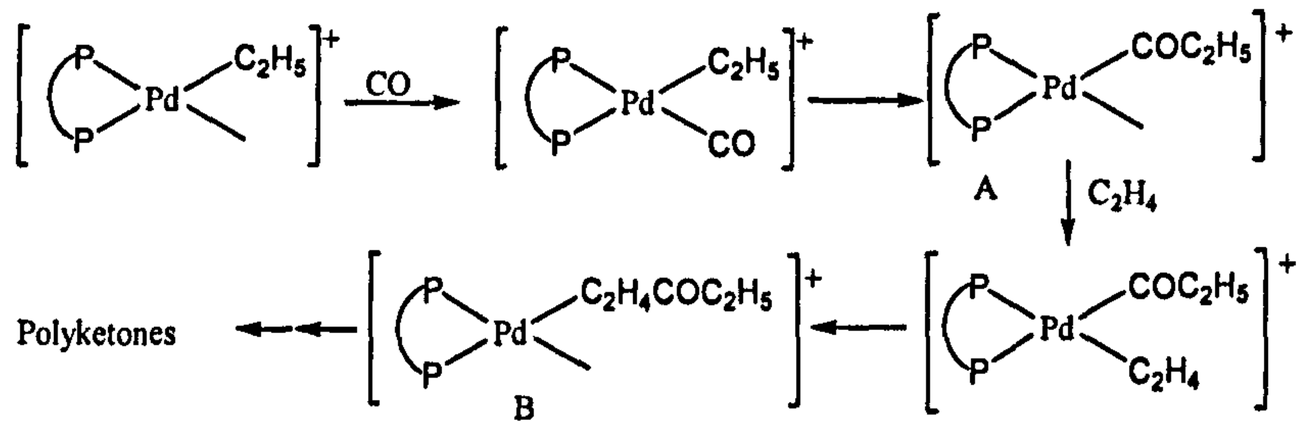


Figure 1- 6: Formation of polyketones

The most efficient catalyst system for the production of polyketones was formed from an equimolar amount of 1,3-bis(diphenylphosphino)propane dppp and $[Pd(OAc)_2]$ upon the addition of 2 equivalents of a Bronsted acid, such as HBF_4 or TsOH.[18]

There are two possible cycles by which CO-ethene polymerisation can occur. These are the carbomethoxy and the hydride cycles. They are described in more detail later in this section. The hydride cycle is initiated by a palladium-hydride complex formed by reaction with MeOH. Termination of the acyl intermediate (A in *Figure 1- 6*) after multiple monomer insertions generates polymeric ketoesters and reforms the hydride complex. Protonation of the palladium-alkyl intermediate (B in *Figure 1- 6*) allows the crossover from the hydride cycle to the carbomethoxy cycle producing diketones (*Figure 1- 7*). The carbomethoxy cycle is initiated by a methoxide complex formed by reaction with MeOH. Termination by protonation of the alkyl intermediate after multiple monomer insertions leads to polymeric ketoesters regenerating the methoxide complex. Crossover between the two cycles can occur again in this case if the acyl complex, A in *Figure 1- 6* is attacked by methanol to give the palladium hydride and diester products. End group analysis of the polyesters formed usually shows that diketones, ketoesters and diesters are formed in a 1:2:1 ratio suggests that the rates of the two cycles are similar and that crossover between them is facile.

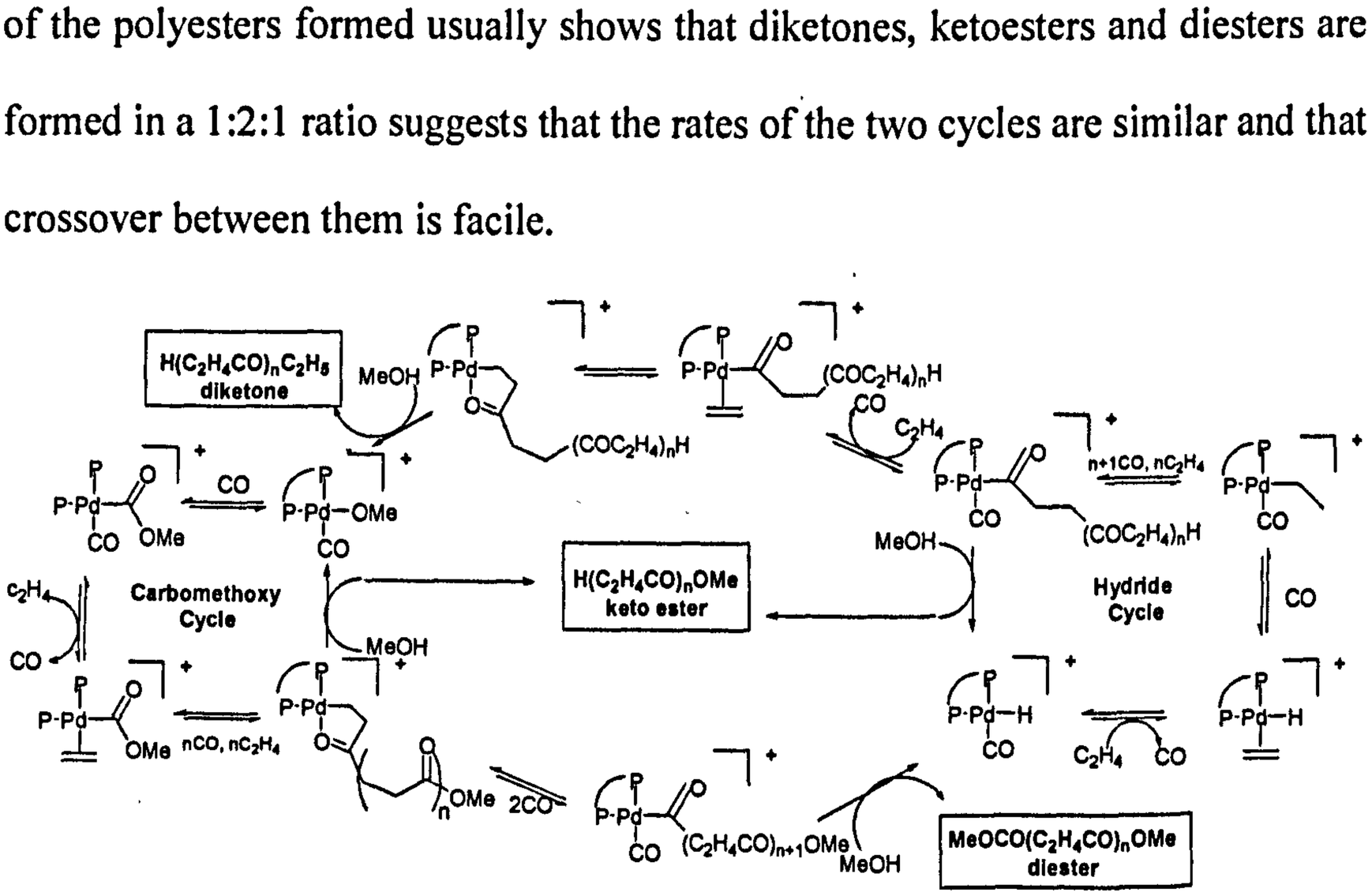


Figure 1- 7: Crossover from the hydride cycle to the carbomethoxy cycle

The high activity displayed by the [Pd(dppp)X_2] system was attributed to optimal stabilisation by this ligand (containing 3 bridging methylenes) of both the square planar ground state and the trigonal bipyramidal transition state which is believed to result during substitution and nucleophilic attack. Efficient catalysis resulted due to the low energy barrier between these two states. The cationic nature of these catalysts prevents strong binding of ethene and CO, which facilitates rapid alternate insertion steps.

Palladium complexes of 1,3-bis(di-*t*-butylphosphino)propane (DTBPP) were, surprisingly, reported to be highly efficient for the selective methoxycarbonylation of ethane.[11] This diphosphine forms cis complexes, which for other bidentate ligands is well known to provide selective formation of polyketone from CO and ethene, since the growing chain and the vacant coordination site are always cis to one another allowing fast migratory insertion. A few years later Tooze reported an increase of the activity (440000 g product $(mol\ cat)^{-1}\ h^{-1}$) and 99.98 % selectivity to methyl propanoate if 1,2-bis(di-tert-butylphosphinomethyl)benzene (DTBPMB) in combination with $Pd_2(dba)_3$ and methane sulphonic acid was the catalytic system.[12]

To gain an understanding of the highly selective formation of methyl propanoate rather than of polyketone achieved when using DTBPMB-Pd complexes, the P-Pd-P bite angle for this system has been studied in great detail, so that structure-property relationships for (P-P)Pd–alkene could be developed.[13] Complexes having this kind of structure exhibit a trigonal planar environment around the palladium, with the bite angle being 104° approximately in all cases (*Figure 1- 8*). Substitution on the ring does not affect the effectiveness of the catalyst, suggesting that the activity of the ligand is provided by the bulky environment of

the phosphine. The nature of the substituents of the phosphine seems to determine an optimum steric environment, responsible for the single or multiple insertion of the alkene prior to termination of the chain.

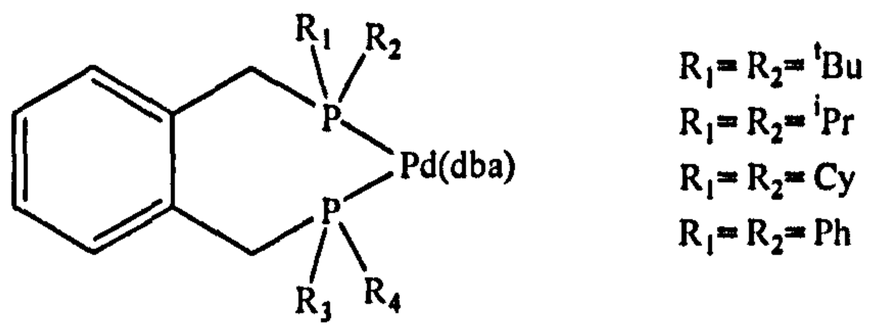


Figure 1- 8: Structure of palladium-DTBPMB and related complexes

Since 1,2-bis(di-*tert*-butylphosphinomethyl)benzene (DTBPMB) and $^tBu_2P(CH_2)_3P^tBu_2$ have unusually high activity for the carbonylation of ethene when using a palladium (0) source such as $Pd_2(dba)_3$, their coordination chemistry to $Pd(OAc)_2$, which is a palladium (II) source has been studied (*Figure 1- 9* and *Figure 1- 10*).[13]

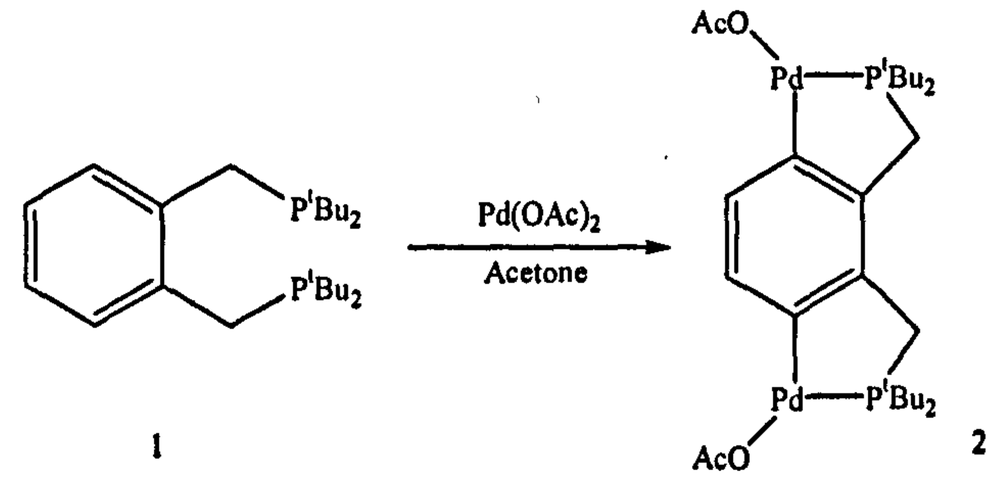


Figure 1- 9: Structure of Pd(II)-DTBPMB complex

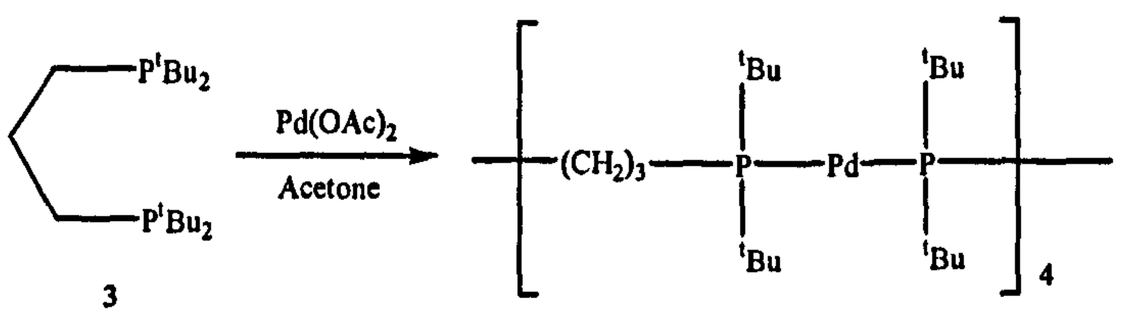


Figure 1- 10: Structure of Pd(II)-dbpp complex.

Products 2 and 4 have been characterised and it has been demonstrated that these ligands do not adopt the typical bidentate chelate structure when using palladium

acetate, but orthometallation occurs. However, when using Pd(0) or $PdCl_2$ bidentate coordination is achieved.

Mechanistic studies on ethene carbonylation

As indicated above, two mechanisms have been proposed to be operating in the methoxycarbonylation of ethene. The carbomethoxy mechanism (*Figure 1- 11*) involves initial formation of a methoxycarbonyl complex either by migratory insertion of CO into a Pd-OMe bond or by nucleophilic attack of methanol on coordinated CO, followed by coordination and insertion of ethene and methanolysis. This mechanism operates when [Pd(1,3-bis(diphenylphosphino)propane] complexes are present. Insertion of ethene onto the Pd-COOMe bond followed by methanolysis releases methyl propanoate.[15] Cole-Hamilton and coworkers have recently shown that this mechanism can also operate in the formation of methyl propanoate and methyl propenoate from CO, ethene and methanol catalysed by rhodium complexes containing electron donating β-ketophosphine and related ligands.[23]

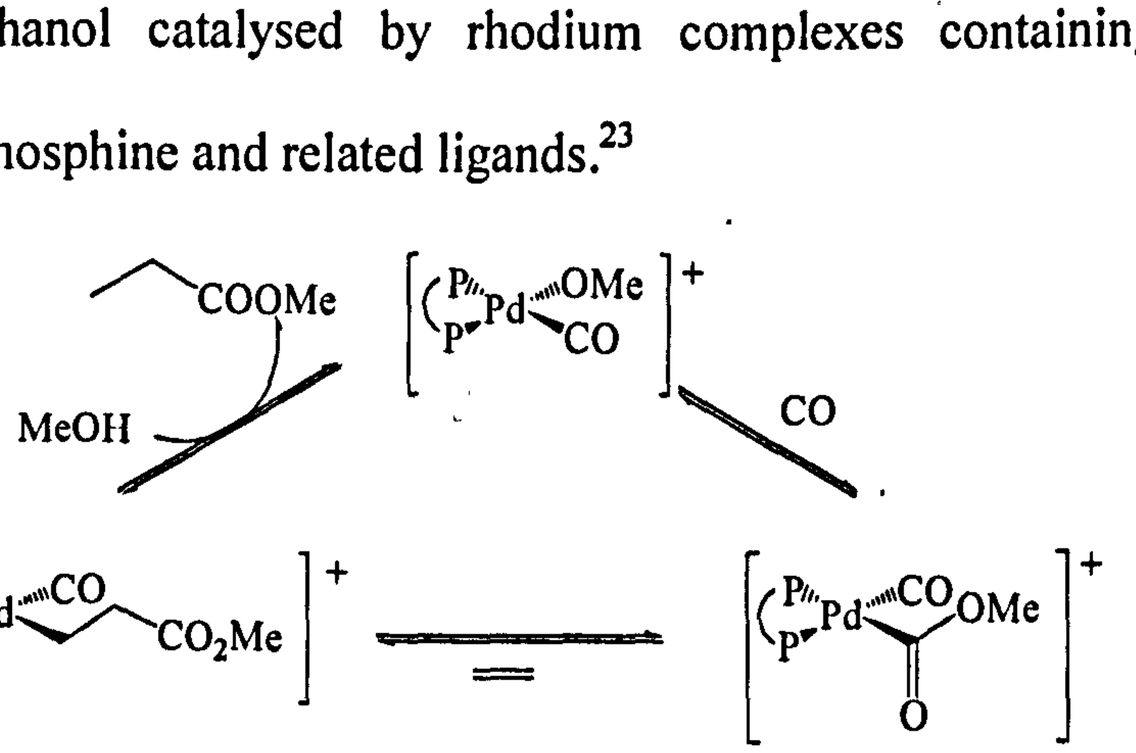


Figure 1- 11: Carboxymechanism for the methoxycarbonylation of ethene

The hydride mechanism (*Figure 1- 12*) starts with a CO-Pd-hydride species. A molecule of ethene replaces the coordinated CO and migration of the hydride onto the coordinated alkene leads to the formation of a Pd-alkyl species. The vacant site left is then occupied by CO, to which the alkyl group migrates to form a Pd-

acyl species. Methanolysis of this species releases methyl propanoate.[15] This mechanism has been proven to be operating in the polyketone formation as well as in the methoxycarbonylation of ethene[20,22] and all the species involved in this mechanism have been synthesised and characterised, confirming that DTBPMB coordinates the metal centre in a bidentate cis fashion in all the intermediates.[15, 17, 20] Measurements of the methanolysis of the Pd-acyl species have been carried out.[21] The complex [(DTBPMB)Pd($COCH_3$)(O_2CCF_3)] was synthesised in order to obtain further information on the methanolysis step. Surprisingly, it exhibits extremely high reactivity towards methanol even at -90 °C to produce a palladium-hydride, zerovalent palladium and a palladium-hydride-carbonyl dimer in addition to methyl acetate. This finding suggests that a vacant site cis to the acyl and steric bulk around the metal are necessary for fast alcoholysis to occur.

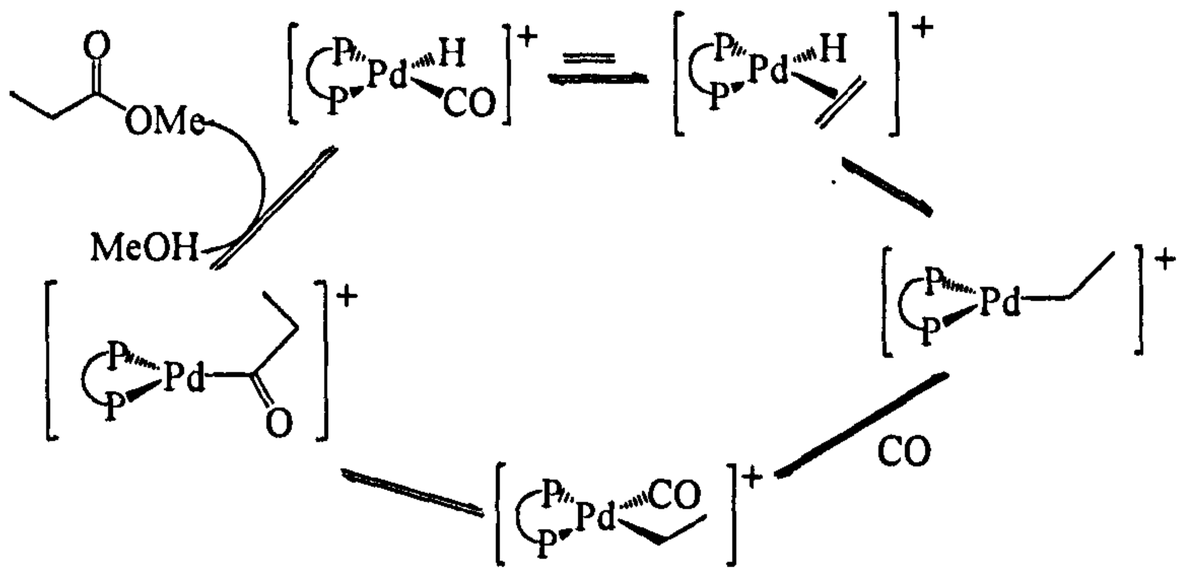


Figure 1- 12: Hydride mechanism for the methoxycarbonylation of ethene

It has been shown that the migratory insertion of CO into the Pd-alkyl intermediate is fast and reversible and DTBPMB appears to promote fast methanolysis of the Pd-acyl so formed to give methyl propanoate.[21] There are three proposed mechanisms for the methoxycarbonylation of alkenes:

a. Drent.

It is well known that DTBPMB and DTBPP allow very fast methanolysis of the palladium-acyl intermediate formed in the catalytic cycle. The basic phosphine-palladium intermediate polarizes the methanol O-H bond favouring the nucleophilic attack of methoxide on the acyl and regenerating the Pd-hydride by protonation (*Figure 1- 13)*.

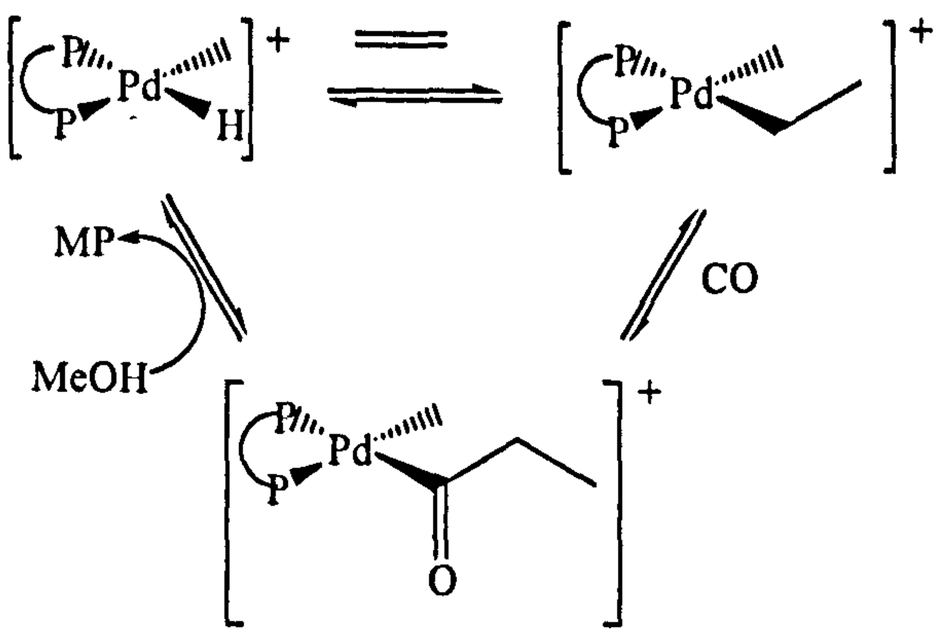


Figure 1- 13: Mechanism proposed by Drent for the production of methyl propanoate

b. van Leeuwen.

Ligands DTBPP and DTBPMB have very bulky substituents on the phosphorus and they have wider bite angles than other ligands, like dppp or dppe. It has also been shown spectroscopicaly that all the intermediates involved in the hydrido mechanism contain a diphosphine ligand coordinated in a cis fashion.

Van Leeuwen and coworkers have investigated the reactivity of a series of diphosphines which coordinate the metal centre in a *trans* mode, such as DPEphos or SPANphos.[34] Acetyl palladium complexes *cis*-[(L)PdC(O)CH_3(CH_3O)] of these ligands lead to the fast formation of methyl acetate. However, the use of other alcohols, like phenols, produced the corresponding *cis*-[(L)PdC(O)CH_3(OAr)], which underwent fast reductive elimination of aryl acetate when the alcohol used was a strong nucleophile. *Trans*-[(PEt_3)$_2$PdC(O)CH_3(OAr)]

did not undergo reductive elimination of the ester. SPANphos and dtbpf coordinate the metal centre only in *trans* fashion and no methanolysis was observed whatsoever. Nevertheless, diphosphines which coordinate the metal in a *trans* mode can temporarily adopt cis coordination leading to methanolysis to form the ester. These observations led them to conclude that cis to the acyl group a vacancy is needed for a coordinating alcohol and that steric bulk accelerates reductive elimination of the ester (*Figure 1- 14*).

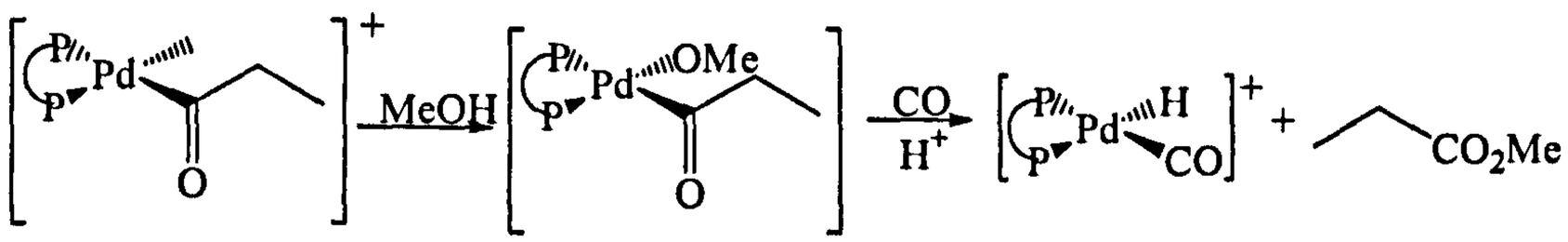


Figure 1- 14: Reductive elimination of methyl propanoate

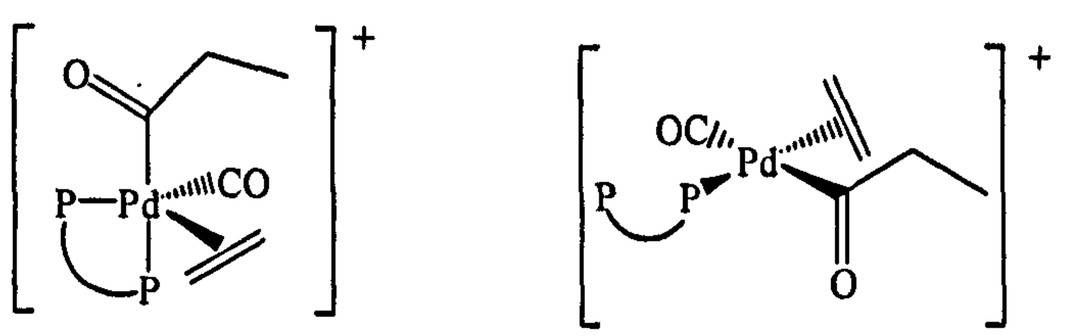
It is not clear, however, why methoxide should attack the very highly electron rich centre in the Pd-DTBPMB so much faster than in any of the other less electron rich complexes. The conclusion that sufficient steric bulk of a cis coordinating ligand can lead to fast elimination to ester formation leaves another possible mechanism, in which one end of the bidentate ligand dissociates before the ester formation takes place. Reductive elimination leading to ester formation seems to be favoured by a strained, bulky cis complex.

c. Eastham.

The high selectivity of MEP formation when using DTBPMB or DTBPP might imply that DTBPMB and DTBPP are unidentate from very early in the reaction, and indeed unidentate coordination has been observed for DTBPP. NMR studies have shown that when all observable intermediates in the catalytic cycle using DTBPMB have the ligand bound in a bidentate fashion.

Kinetic analysis and deuterium labelling have shown that the mechanism of formation of MEP in the DTBPMB system involves the hydride cycle and the rate determining step might be attack of methoxide onto the coordinated acyl intermediate.

The very highly electron density on the metal when using the highly electron donating diphosphines DTBPP and DTBPMB would tend to disfavour the nucleophilic attack of methanol and it is difficult to explain, on this basis, the very high rate and selectivity towards MEP. It is proposed that the diphosphine becomes unidentate at this point in the first catalytic cycle (*Figure 1- 15*). This would probably happen by direct decomplexation to give a three coordinate intermediate, with dissociation of the phosphorus *trans* to the acyl group, which has a very high *trans* influence and hence also a high *trans* effect in dissociative processes or it might occur via an associative process with CO or alkene promoting the reaction. In such an associative process complex A is likely to be formed, with one P, the leaving group (CO) and the incoming group (the alkene) in the equatorial plane. Once this intermediate is formed, the most energetically favourable pathway may lead to loss of a P atom rather than the expected CO and to the formation of complex B.



Complex A Complex B

Figure 1- 15: Mechanism proposed by Eastham for the production of methyl propanoate

Either of these pathways to decomplexation of one P atom of the bidentate diphosphine leads to an intermediate that has much lower electron density on the

metal than those containing the diphosphine with a bidentate binding mode, so that nucleophilic attack of methanol will be much faster.

Macgregor and coworkers[35] have carried out computational studies (using Tinker as a molecular mechanics program) for the methoxycarbonylation of ethene using four systems of the general form $[(P\text{-}P)Pd\{C(O)Et\}(CO)]^+$, where P-P = 1,2-diphosphinoethane (DHPE), 1,2-diphosphinopropane (DHPP), 1,2-diphenylphosphinopropane (DPPP) and 1,2-ditertbutylphosphinopropane (DTBPP). These calculations do not take into account the electronic effects of the phosphine substituents. The results they found provide further support for the hypothesis that a phosphine may become unidentate.

They studied the pathway for ethene addition to the complex $[Pd(DTBPMB)(COEt)(CO)]^+$ to give a pentacoordinated intermediate and also the energy associated with decoordination of one phosphine arm to give a tricoordinated species (*Figure 1- 16*). The behaviour of the DHPE and DHPP systems were very similar to another. Ethene coordinates the palladium hydride species to give the pentacoordinate intermediate with no cost in energy. This species has the ethene lying in the equatorial plane. The calculated enthalpy change is around -8 to -9 kcal mol^{-1} and once thermal and entropy corrections are included the free energy change is more like + 5 or 6 kcal mol^{-1}. This situation is more favourable than loss of one phosphine arm which costs approximately +21 kcal mol^{-1} (ΔH) or ca. +17 kcal mol^{-1} (ΔG).

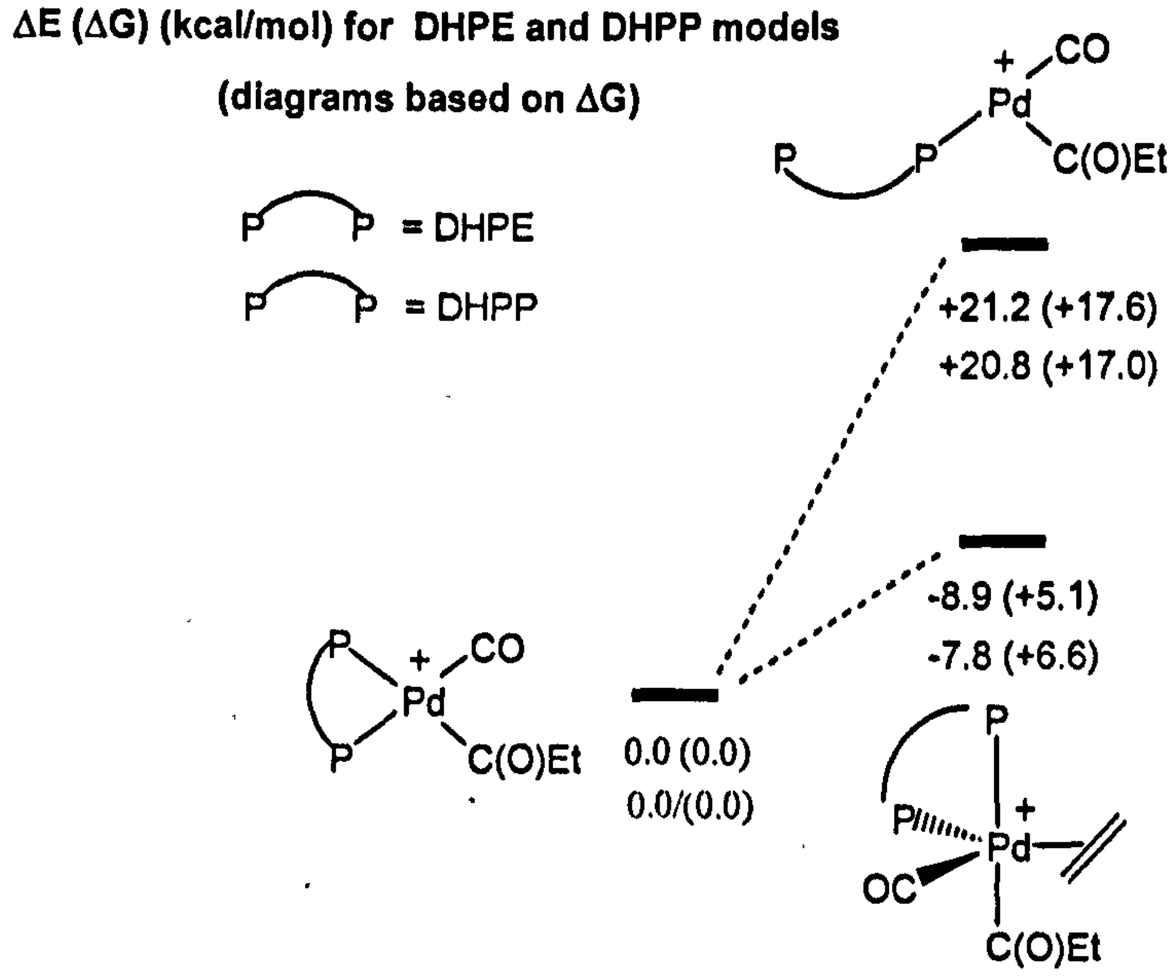


Figure 1- 16: Calculated energy barrier for the coordination of ethene when DHPE or DHPP are the ligands

For DPPP and DTBPP there is now a barrier to ethene addition. For DPPP this is very small and the transition state is barely above the pentacoordinate intermediate formed. In this case ethene addition is still very much more favourable than phosphine arm loss (*Figure 1- 17*). However, for DTBPP the situation is different. The tricoordinate species formed via phosphine arm loss is more accessible, +14.1 kcal mol^{-1} (ΔG), than the pentacoordinate intermediate, +15.0 kcal mol^{-1} (ΔG), which requires an activation free energy of +20.7 kcal mol^{-1}. Indeed, in $[Pd(DPPB)(CO)(COEt)(C_2H_4)]^+$, one Pd-P distance is 3.9 Å, the phosphine arm *trans* to the acyl is in fact completely dissociated and the metal is tetracoordinate with the acyl group axial and CO, ethene and the other P in the equatorial positions. Preliminary studies on the transition states involved in the process of dissociation of one phosphine arm based on a lengthening of the Pd-P bond suggest that the actual tricoordinate species is not energetically disfavoured compared to the tetracoordinate species which has a long Pd-P bond. However, the reason for the anomalously high energy required for the dissociation of one

arm of DPPP remains unclear. Alkene addition to the tricoordinate intermediate to form the tetracoordinated species when DHPE, DHPP and DPPP are the ligands occurs *trans* to acyl, as expected for a pseudo-square planar structure.

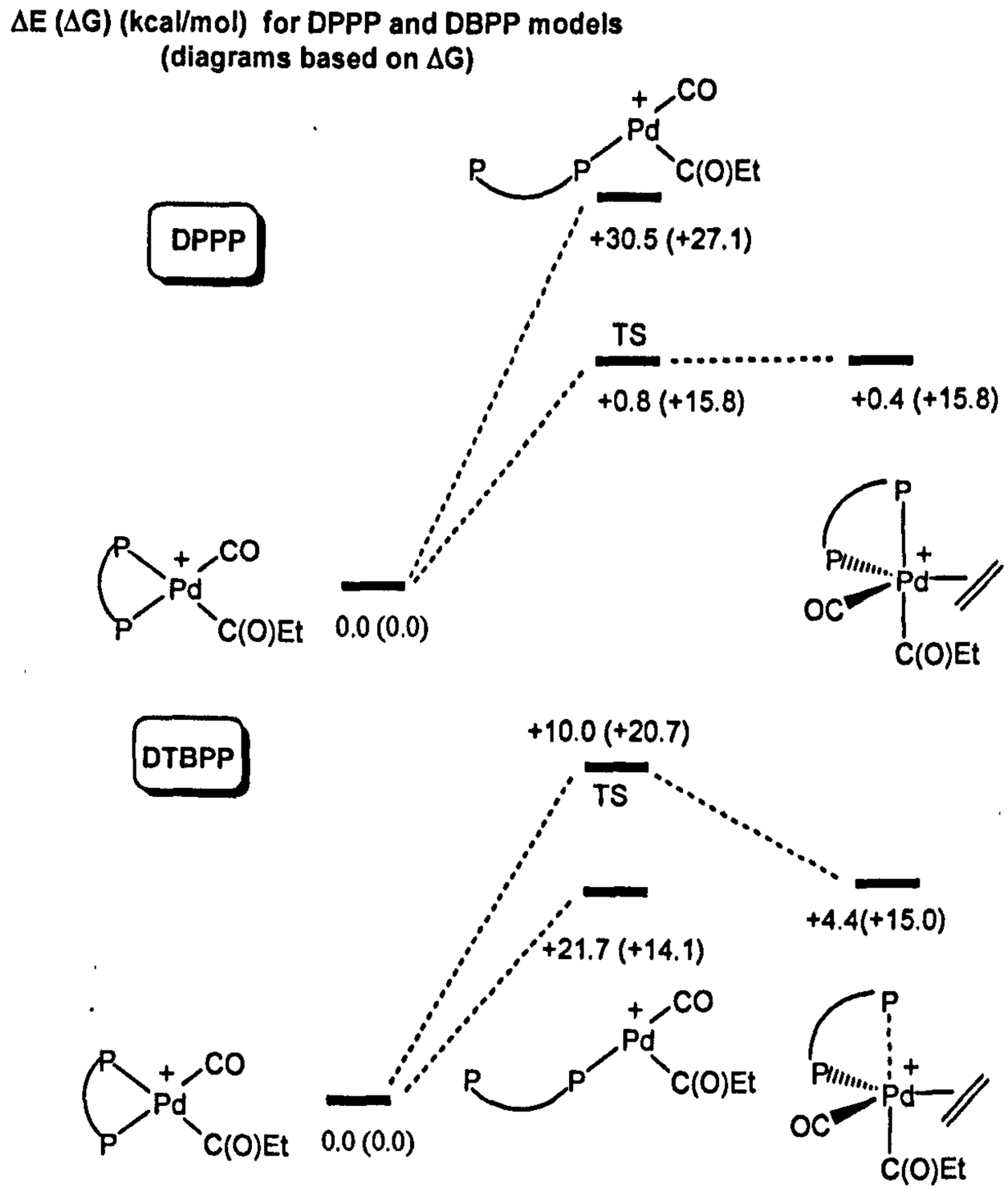


Figure 1- 17: Calculated energy barrier for the coordination of ethene when DPPP or DTBPP are the ligands

The first sixteen electron, trigonal planar palladium carbonyl complex has been reported by Bellabarba.[14] Reaction of $[PdCl_2(DTBPMB)]$ and CO in ethanol yielded yellow crystals of [Pd(CO)(DTBPMB)]. This complex was fully characterised by IR, NMR and X-ray crystallography. The IR spectrum showed a band at 1959 cm^{-1}, typical of terminal carbonyls, which was surprising since this sort of complex tends to form bridging structures. However, in this case, due to the bulk of the ligand the monomer is stable. The ^{1}H and ^{31}P NMR showed the

expected peaks. The presence of MeOH did not form the expected hydrido-carbonyl complex even in the presence of acid.

1.1.2.1. Effect of oxygen and acid.

The complex [Pd(DTBPMB)(dba)] reacts in MeOH with HBF_4 or CF_3SO_3H (TfOH) in the presence of oxygen or benzoquinone (BQ). A new compound is formed selectively: [Pd(DTBPMB)H(MeOH)]X. Palladium-hydrides are usually quite reactive and unstable, especially in the presence of labile ligands, such as weakly coordinating solvent molecules. However, the complex mentioned above has been fully characterised and it has be shown to be a key intermediate in the catalytic cycle[17]. NMR data for this complex show two different resonances for the P atoms. In addition, the chemical shift of the P atom cis to the H shows a strong dependence on the solvent, suggesting that a solvent molecule occupies the fourth coordination site. The formation of this sort of hydride from [Pd(DTBPMB)(dba)] requires the presence of a primary or secondary alcohol as well as the presence of an acid and an oxidant, such as oxygen or BQ. The oxidant can be added to the starting Pd (0) complex [Pd(DTBPMB)(dba)], since the complexes [Pd(DTBPMB)(μ^2-O_2)] and [Pd(DTBPMB)(μ^2-BQ)] react with an alcohol to give the hydride [Pd(DTBPMB)(dba)]. On the other hand, [Pd(DTBPMB)(dba)] does not form [Pd(DTBPMB)H(MeOH)]X when TfOH is present in the absence of an oxidant. This reaction leads to the protonation of coordinated dba. Crystal structures of [Pd(DTBPMB)(μ^2-O_2)] and [Pd(DTBPMB)(μ^2-BQ)] have been obtained. In both cases the Pd atom has a distorted square planar geometry. The role of the alcohol is to provide the hydrogen atom that would act as hydride. It has been found that the hydride is

only formed when a primary or a secondary alcohol are used, whereas with tertiary alcohols or non-alcoholic solvents the hydride complex is not formed. The only primary alcohol not forming the hydride was CF_3CH_2OH. The hydride is formed by β-elimination from a molecule of solvent coordinated to the palladium centre and consequent oxidation of the alcohol to aldehyde or ketone. In the case of CF_3CH_2OH the failure to form the hydride must be related to the more difficult β-elimination because of the very electron withdrawing groups present (these groups make the oxidation more difficult).

It is possible to form the hydride in the presence of a non-alcoholic solvent (THF, acetonitrile, etc) by removing MeOH from a solution of $[Pd(DTBPMB)(\eta^1\text{-}TfO)_2]$ and adding the corresponding solvent. These complexes have been fully characterised by NMR and once more it was found that the chemical shift of the P cis to the H is strongly dependent on the solvent. When the reaction was carried out in a dry non-alcoholic solvent, the product observed was $[Pd(DTBPMB)(\eta^2\text{-}TfO)]^+$. When oxygen is bubbled through a solution of [Pd(DTBPMB)(dba)] in MeOH for 20 minutes at room temperature in the presence of TfOH, the complex [Pd(DTBPMB)H(MeOH)]X was formed in a clean reaction. The addition of 1-7 moles of BQ per mole of palladium to a solution of [Pd(DTBPMB)(dba)] in methanol in the presence of TfOH gave complex [Pd(DTBPMB)H(MeOH)]X in a few minutes (*Figure 1- 18*). Metallation of the phosphine, which a known unusually promoted by oxidants reaction, is not observed.

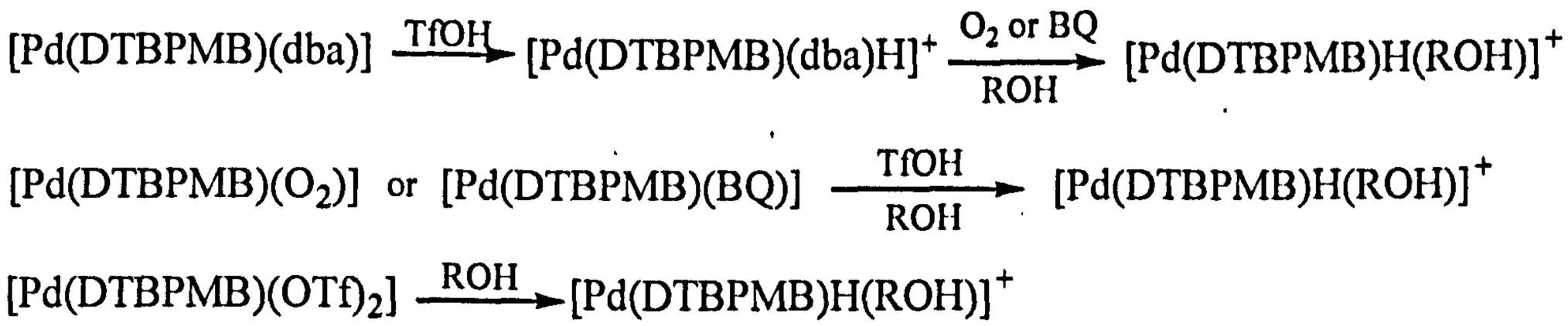


Figure 1- 18: Formation of [Pd(DTBPMB)H(ROH)]

Ligand variation dramatically affects the chemoselectivity of the reaction between CO and ethene from production of polyketone to the production of methyl propanoate. Likewise, a variation in the acid changes the chemoselectivity of the reaction. Strongly coordinating anions (halides) lead to stable complexes and therefore inactive catalysts for methoxycarbonylation. Hence, the anion must be easily displaced by the reactants. For DTBPMB the formation of [Pd(DTBPMB)H(MeOH)]X from [Pd(DTBPMB)(dba)] in MeOH and TfOH has been demonstrated. The choice of the acid is important here also, since if the anion is strongly coordinating, it will coordinate the metal. For instance, the use of HCl or CF_3CO_2H (TFA) gives [Pd(DTBPMB)Cl_2] and [Pd(DTBPMB)(O(O)CCF_3)], respectively. On the other hand, when HBF_4 is the acid, the hydride [Pd(DTBPMB)H(MeOH)]X is formed. However, the same reaction carried out in the presence of $MeSO_3H$ or TsOH, yields the unexpected complexes [Pd(DTBPMB)(η^2-$MeSO_3$)]$^+$ and [Pd(DTBPMB)(η^2-TsO)]$^+$ instead of the analogous η^1 complex (*Figure 1- 19*).

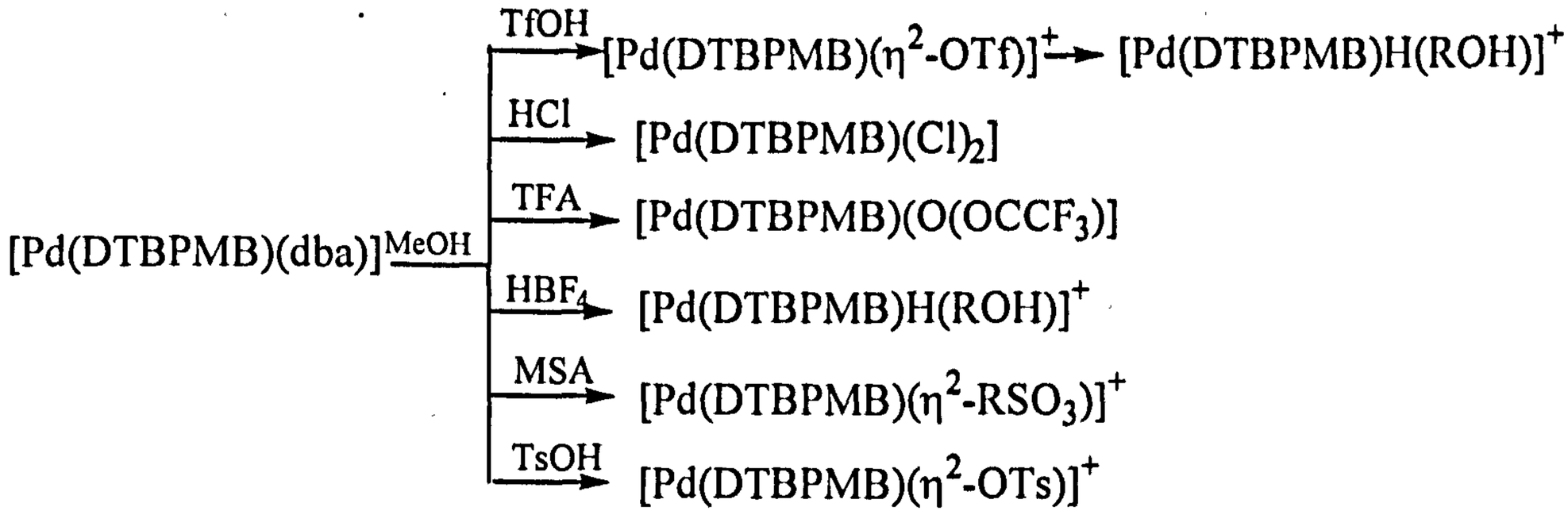


Figure 1- 19: Reaction of [Pd(DTBPMB)(dba) with different acids

These two complexes are structurally analogous to $[Pd(DTBPMB)(\eta^2\text{-}TfO)]^+$, but their chemistry is very different, since $[Pd(DTBPMB)(\eta^2\text{-}TfO)]^+$ is only observed in non-polar or weakly polar solvents whereas $[Pd(DTBPMB)(\eta^2\text{-}MeSO_3)]^+$ and $[Pd(DTBPMB)(\eta^2\text{-}TsO)]^+$ are stable in MeOH, THF, DCM, methyl propionate and acetone (partial dissociation occurs in acetonitrile). The different behaviour of $[Pd(DTBPMB)(\eta^2\text{-}TfO)]^+$, $[Pd(DTBPMB)(\eta^2\text{-}MeSO_3)]^+$ and $[Pd(DTBPMB)(\eta^2\text{-}TsO)]^+$ may be related to the different strength of coordination of the anion to the metal, since TfO^- coordinates less strongly the metal than $MeSO_3^-$ or TsO^-. In fact, the former dissociates in the presence of a polar solvent to give $[Pd(DTBPMB)(solv)_2]^{2+}$, which can react to form the hydride. On the other hand, the use of $MeSO_3H$ or TsOH requires more severe conditions for partial dissociation to occur and form the hydride. Only in acetonitrile is some dissociation observed. The addition of pyridine makes the hydride formation easier. As it is a strongly coordinating ligand, it forces the acid to change from η^2 to η^1 coordination. The extra stabilisation *via* the chelate effect disappears so the replacement of the anion by MeOH takes place easily as does the formation of the hydride. There are two more ways of obtaining the hydride: a) adding MeOH to the complex $[Pd(DTBPMB)(MeOH)]^{2+}$ and b) thermal activation of

$[Pd(DTBPMB)(\eta^2\text{-}MeSO_3)]^+$ or $[Pd(DTBPMB)(\eta^2\text{-}TsO)]^+$. Therefore, the hydride can be formed in the presence of $MeSO_3H$ at the temperatures required in an industrial process.

Summarising, the hydride formation does not take place in a simple single step. In fact, it involves four sequential steps (*Figure 1- 20*):

1. Protonation of 1 to give $[Pd(DTBPMB)(dbaH)]^+$
2. Oxidation of $[Pd(DTBPMB)(dbaH)]^+$ by oxygen or benzoquinone to give $[Pd(DTBPMB)(\mu^2\text{-}RSO_3)]^+$. Under the operating conditions of temperature this step only requires traces of oxygen to be induced.
3. Displacement of the $RSO_3^{\bullet}$ by the solvent to form $[Pd(DTBPMB)(solv)_2]^{2+}$, which is favoured in polar solvents. Basic R groups disfavour this step.
4. Irreversible β-hydride elimination from a primary or secondary alcohol coordinated to the metal.

Methanol has more than one role in the methoxycarbonylation of ethene:

1. It is a reagent in the formation of methyl propanoate.
2. It is involved in the formation of the hydride (2).
3. It stabilises the hydride by solvating the ionic species.

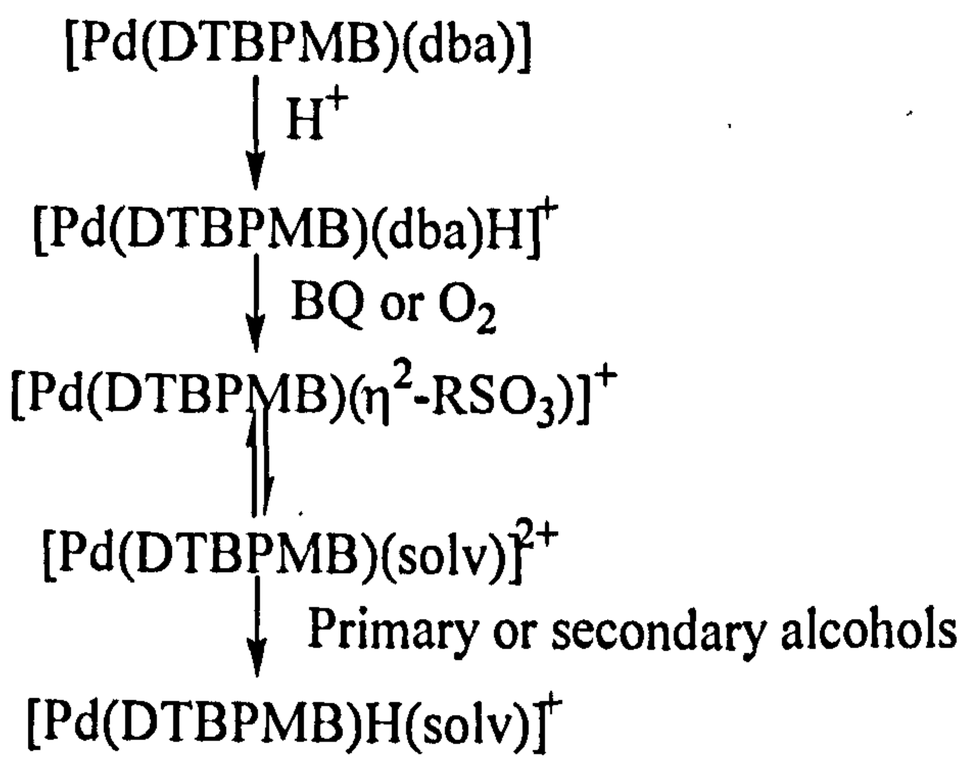


Figure 1- 20: Formation of the palladium-hydride

The use of DTBPMB in other catalytic reactions

Recently a patent by Drent[16] describes a process for the carbonylation of ethylenically unsaturated linear or branched substrates having preferentially 4-14 carbon atoms using DTBPMB and a $Pd(OAc)_2$ as a source of cationic Pd^{II}. The examples shown in the application are 1-octene, 2-octene and methyl-3-pentenoate. An acid is required in this system, with sulphonic acids being particularly preferred. The molar ratio of the source of anions and palladium used varies from 1:1 to 5:1.The application also specifies in the examples shown that an aprotic solvent must be used. Suitable temperatures and pressures conditions are claimed. Temperatures in the range of 50-250 ^{0}C and pressures in the range of 1-100 bar are claimed although the range of 80-120 ^{0}C and of 1-65 bar are preferred. All the examples shown are carried out at 100 ^{0}C under 20-60 bar of CO. Under these conditions they claim 100 % conversion and 97.5 % selectivity to the linear ester regardless of where the initial double bond is in the alkene.

The remaining chapters of this thesis outline studies aimed at the catalytic applications of DTBPMB as a ligand.

1.1.3. References

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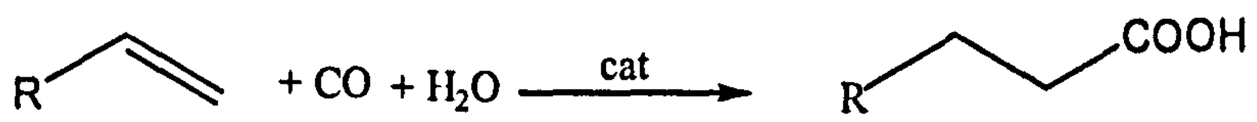
Chapter 2:

METHOXYCARBONYLATION OF ALKENES

2.1. Methoxycarbonylation of alkenes.

In the carbonylation method developed by Reppe, carbon monoxide is allowed to react with organic compounds such as alkynes, alkenes, alcohols, ethers and esters under the catalytic influence of metal carbonyls and carbonyl metal hydrides. The carbonylation of unsaturated compounds usually involves the participation of compounds having an acidic hydrogen such as water, alcohols, thiols, ammonia, amines or carboxylic acids. The end products are carboxylic acids and their functional derivatives. Unsaturated products are obtained from alkynes while saturated products are obtained from alkenes (*Scheme 2- 1*).[1]

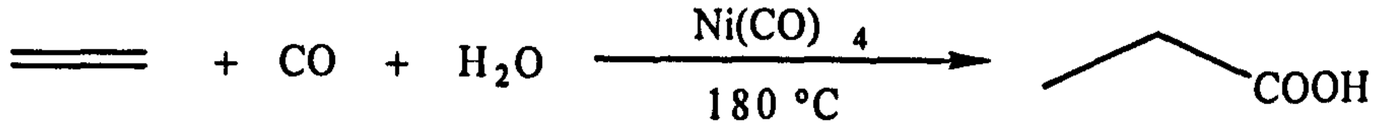


Scheme 2- 1: Hydrocarbonylation of alkenes

The early carbonylations of alkenes in the presence of water or alcohol were carried out at high temperature (300 °C) and high pressure (700-900 atm) and the catalysts could be phosphoric acids, heteropolyacids, boron trifluoride or metal halides. Metal carbonyls were often regarded as reaction inhibitors but Reppe's experiments with acetylene and carbon monoxide showed that metal carbonyls and carbonyl metal hydrides are excellent carbonylation catalysts, which are effective at lower temperature.[1] Metal carbonyls proved to be superior to earlier catalytically active systems, in particular where strong acids were used because the pressures and temperatures that had to be applied led to isomerisation of the substrates and resulted predominantly in the formation of branched isomers of carboxylic acids. Metal carbonyls were of great advantage over the older catalysts in this respect. It was possible to optimise the catalyst metal, the ligands and the

promoters for nearly every carbonylation reaction, allowing the reaction to take place under milder conditions and with greater selectivity to the desired linear products than had been observed previously.[2]

Reppe's first catalytic carbonylation was the reaction of acetylene with CO and H_2O under pressure to form acrylic acid; nickel carbonyl was used as the catalyst. This reaction proceeded under relatively mild conditions (about 300 atm and 170 °C). Esters of acrylic acid were obtained under the same conditions from acetylene, CO, and alcohols in the presence of halides of metals that form carbonyls, for example, $NiBr_2$ and NiI_2. The next step was to attempt to prepare propanoic acid and its esters by the catalytic reaction of ethene with CO and water or alcohols.[1] Propanoic acid is produced by the carbonylation of ethene, which is reacted exothermically with carbon monoxide and water. $NiCl_2$ was patented as early as 1943 as a catalyst for the carbonylation of ethene (*Scheme 2- 2*).



Scheme 2- 2: Synthesis of propionic acid

The catalyst is a nickel hydride complex that is generated under the reaction conditions (100-300 bar and 250-320 °C) by reduction of the nickel salt to give $Ni(CO)_4$ as a precursor. In principle the same catalytic systems that can be used for the carbonylation of ethene to propanoic acid are applicable for the synthesis of higher carboxylic acids from alkenes. Higher alkenes show distinct chemical and physical differences from ethene. These result in a number of obstacles when producing carboxylic acids from them. Additionally, the hydrocarbonylation of higher alkenes gives mixtures of the linear and branched acids. Selectivities are in

general low due to the facile double-bond isomerisation by the carbonylation catalysts.[2]

2.1.1. Palladium complexes as catalysts for hydroxycarbonylation and methoxycarbonylation of alkenes.

Transition metal-catalysed carbonylation of organic substrates represents a very important process in organic synthesis. Carbon monoxide can be directly introduced into unsaturated substrates to produce organic molecules. Although many transition metals are effective catalysts for the carbonylation, palladium complexes are the most widely employed.

Due to the interest in the synthesis of the anti-inflammatory drugs ibuprofen and naproxen, the hydroesterifications of styrene and vinylnaphtalene derivatives to give branched products have been extensively studied. Cationic palladium complexes have been used for the hydorcarboxylation of styrene. Traditionally, the use of monophosphines led to fast catalysis and selective formation of the branched product whereas the use of diphosphines led to slow catalysis and selective formation of the linear product. Sheldon and coworkers reported 73 % selectivity to the branched product by the use of palladium-tppts at 65 °C, achieving 49 mol (mol of catalyst)$^{-1}$ h^{-1} as the turnover frequency.[3] The use of $[Pd(MeCN)_2(PPh_3)_2](BF_4)_2$ under 5 bar of CO and 80 °C led to the formation of the linear ester as the main product (b:l= 27:73). The cationic palladium complex formed *in situ* from $Pd(OAc)_2$–PPh_3-CF_3SO_3H at 50 °C and 20 atm of CO produced the branched ester as the major product (b:l= 75:25). The active catalyst system in this case was formed *in situ* from these three starting materials when mixed in a ratio of 1/4/10 (*Scheme 2- 3*). Moreover, at room temperature and using

p-TsOH as the acid, the branched product was formed regioselectively (b:l= 93:7).[4]

$$Pd(OAc)_2 + 2\ PPh_3 + 2\ TsOH \longrightarrow Pd(OTs)_2(PPh_3)_2 + HOAc$$

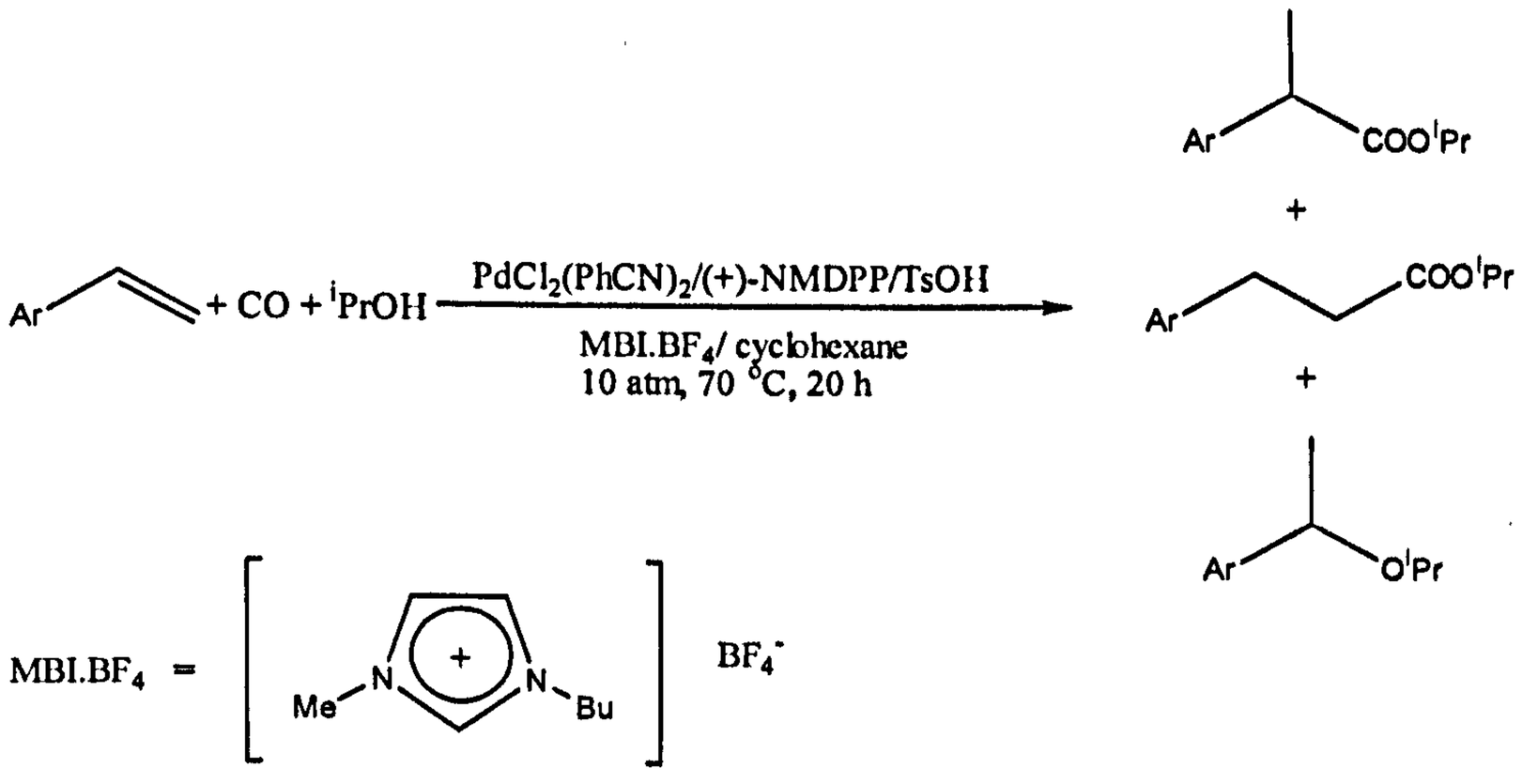
Scheme 2- 3: Pd (II)-PPh_3 catalytic system

The immobilisation of $Pd(OAc)_2$ in montmorillonite was studied by Alper[40] . This kind of complex shows enhanced reactivity and better selectivity to the branched product in the hydroesterification of styrene and in other kinds of reaction (*Scheme 2- 4*).

$$PhCH{=}CH_2 + MeOH + CO \xrightarrow[\substack{C_6H_6,\ 24\ h \\ 125\ ^\circ C,\ 40\ atm\ CO \\ Pd/PPh_3/PhCHCH_2\ -1/5/500}]{Pd\text{-}clay,\ PPh_3,\ HCl} PhCH(Me)COOMe$$

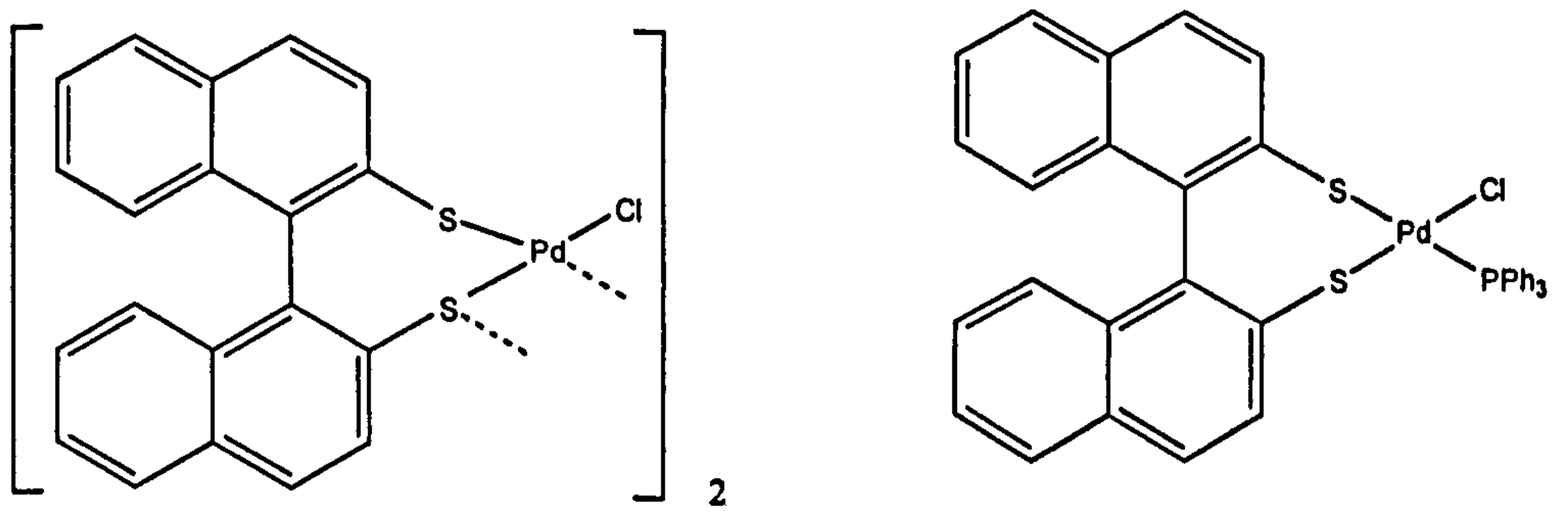
Scheme 2- 4: Hydroesterification of styrene catalysed by Pd-clay

Two-phase catalytic processes, in which the catalytic system can be separated from the products and recycled, have been developed[41]. Composed of a water-soluble palladium complex of trisulfonated triphenylphosphine as the catalyst and a Bronsted acid as the promoter in water or toluene, this kind of catalytic system, when immobilised using 1-n-butyl-3-methyllimidazolium(II)tetrafluoroborate salt as an ionic liquid solvent, gives very good yields and high regioselectivity in the carbonylation of styrene (organic phase) under mild conditions(*Scheme 2- 5*). However, the regioselectivity is very dependant on the phosphine ligand since if (+)-neomethyldiphenylphosphine (NMDPP) is used instead of PPh_3 under these conditions, the regioselectivity increases.



Scheme 2- 5: Alkoxycarbonylation of styrene in ionic liquids

Mono and dinuclear Pd^{2+}-complexes containing thio-thiolether groups were prepared and tested as catalyst precursor in the hydrocarbonylation of styrene.[47] Reaction of RHbinas (R=Me, ^{i}Pr) and $[PdCl_2(PhCN)_2]$ in toluene produces a dinuclear compound, $[PdCl(Rbinas)]_2$ (*Scheme 2- 6*).



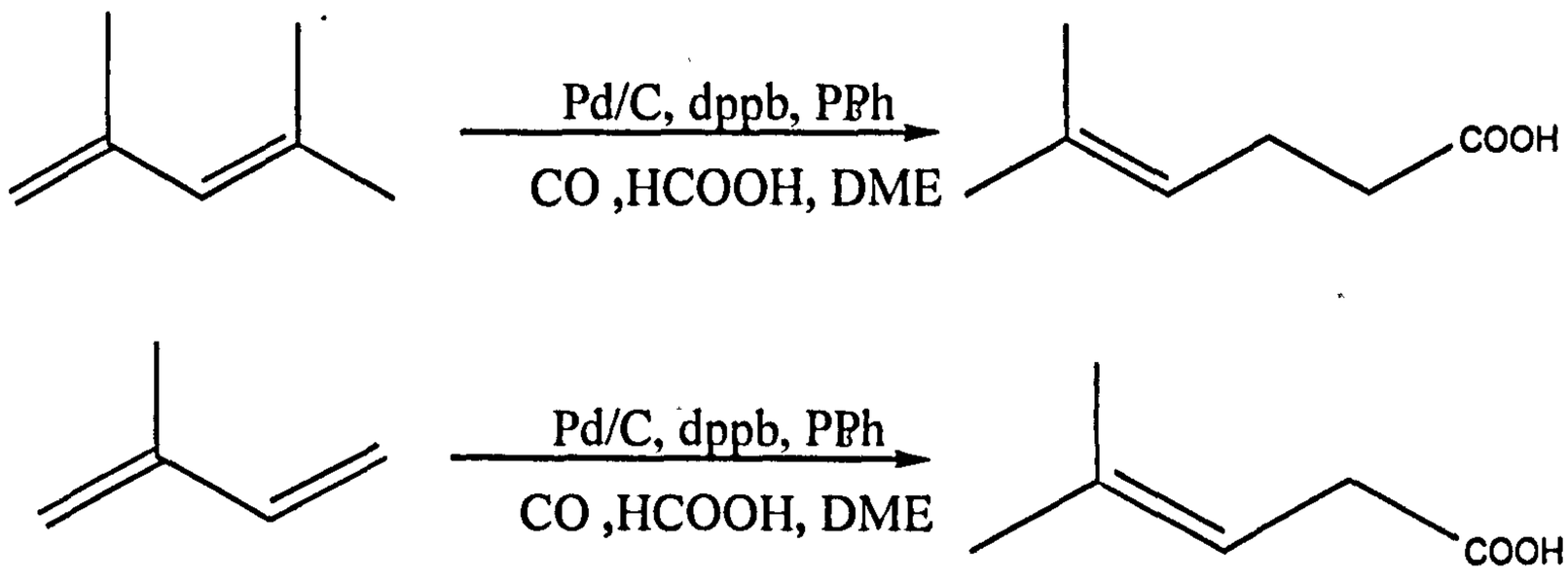
Scheme 2- 6: Structure of $[PdCl(Rbinas)]_2$ and $[PdCl(Rbinas)(PPH_3)]$

By adding PPh_3 in dimethoxyethane this bimetallic complex forms the mononuclear one shown in *Scheme 2- 6*. If R= Me high catalytic activity (90% conversion) and very good regioselectivity to 2-phenylpropanoic acid (89%) are observed at 100°C.

Alper[42] reported a regioselective method for the hydrocarboxylation of substituted styrenes using formic acid, $Pd(OAc)_2$ and 1,4-bis(diphenylphosphino)butane (dppb) in dimethoxyethane under 6-8 atm CO and 150 °C. The major product was

the linear ester under these conditions. Further work of Alper[43] in this area showed that terminal alkenes can also react with formic acid or oxalic acid in the presence of 10% Pd/C and dppb in 1,2-dimethoxyethane providing predominantly the linear product. The reaction conditions are the same as above when using formic acid but if oxalic acid is employed, the CO pressure has to be increased to 40 atm.

A combination of these two systems which contains monodentate and bidentate phosphine was also studied for the carbonylation of conjugated dienes[39] (*Scheme 2- 7*)



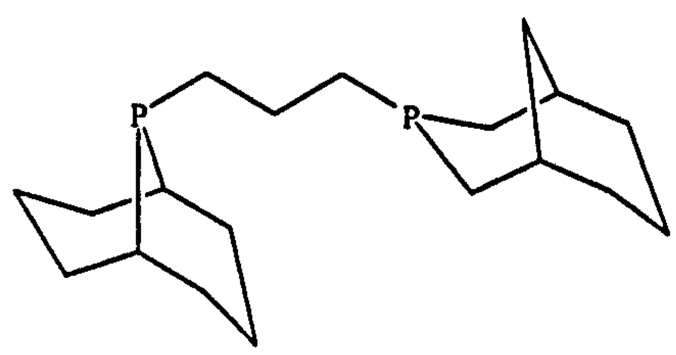
Scheme 2- 7: Carbonylation of conjugated dienes.

When using 2,4-dimethyl-1,3-pentadiene, the γ,δ-unsaturated acid was the only product, while in the case of isoprene the only product was the β,γ-unsaturated acid.

Toniolo has recently reported a turnover frequency of 248 h^{-1} using preformed $[Pd(OTs)_2(PPh_3)_2]$ as the catalyst. Unfortunately, the branched to linear ratio was only 41:59.[5] The highest rate reported so far was obtained employing Xantphos as the ligand.[6]

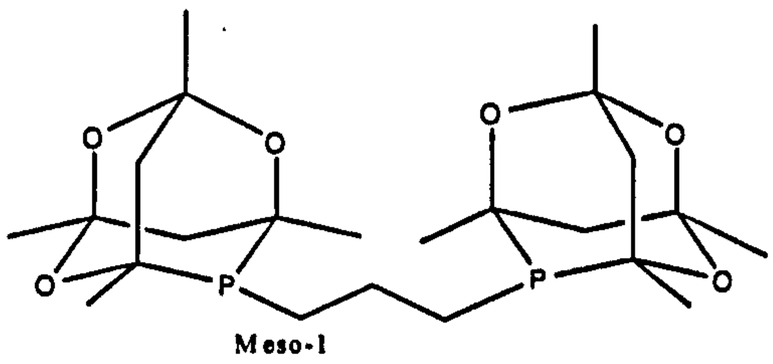
As previously mentioned in chapter 1, the carbonylation of ethene in methanol using palladium based catalysts can lead to polyketones if bidentate phosphines are attached to the palladium centre or to methyl propanoate if unidentate phosphines are employed.[2] Methoxycarbonylation of ethene carried out with a

catalyst based on 1,2-bis(di-*t*-butylphosphino)ethane (DTBPE) results in the formation of diethylketone in 90 % selectivity.[7] Diphosphines based on bicyclononane have also been used for this reaction (*Scheme 2- 8*).[8, 9]

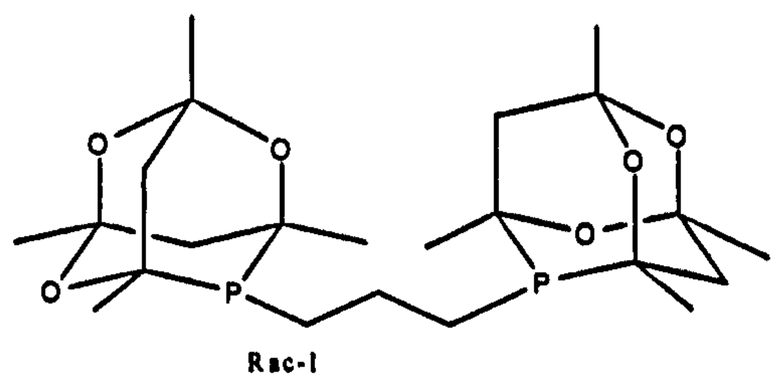


Scheme 2- 8: Structure of 1,3-bis(phosphabicyclononyl)propane

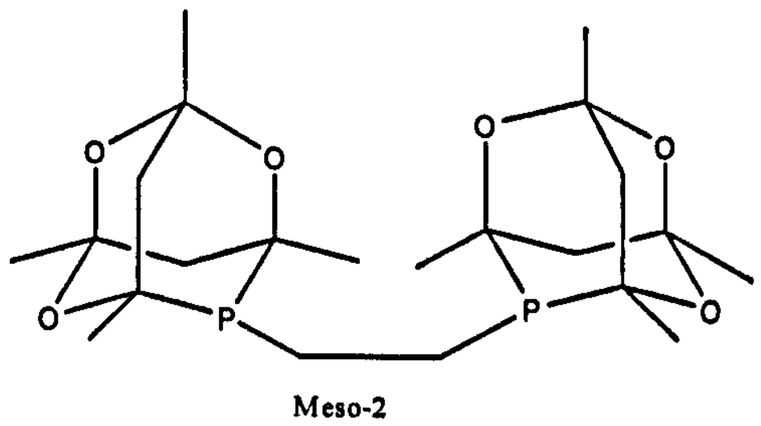
If 1,3-bis(phosphabicyclononyl)propane is used as the ligand in the presence of a non-coordinating anion under 30 bar of CO in MeOH, low molecular weight polymers are formed. However, if the anion is the strongly coordinating propanoate, the product formed is methyl propanoate, suggesting the relevance of the acid employed in the reaction, since strongly coordinating anions appear to inhibit the second insertion of ethene promoting methanolysis of the Pd-acyl complex formed.[10] A recent article showed that palladium (II) complexes containing chelating bis-(phosphaadamantyl)diphosphine (meso/rac-1) (*Scheme 2-9*) catalyses the carbonylation of ethene when combined with $Pd(OAc)_2$ and $MeSO_3H$, achieving activity and selectivity to methyl propanoate similar to those observed with DTBPMB under the same conditions.[11,12,15] After 2 hours the conversion was 93% with 78% selectivity to linear methyl ester at an average rate of 120 h^{-1}. It was found that internal alkenes were selectively converted to linear esters involving tandem isomerisation-carbonylation. Isomerisation was rate limiting and the attainment of the linear isomer as the major product was a consequence of the increased rate of carbonylation at the terminal olefinic position. In contrast, complexes formed by ligands meso/rac-2 (*Scheme 2- 9*) led to the formation of low molecular weight polymers.



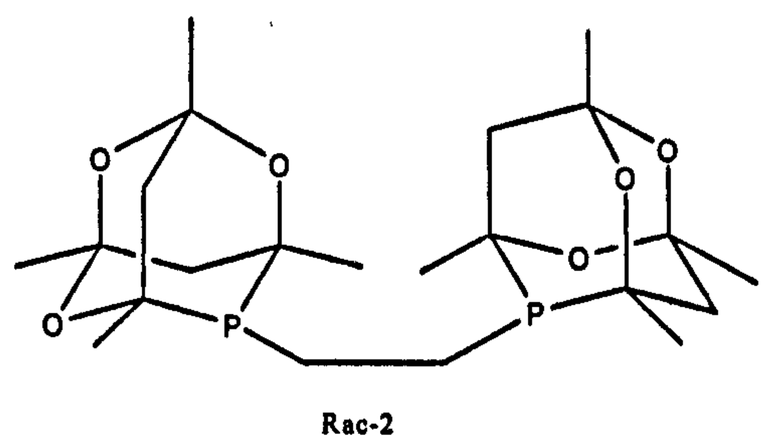
Meso-1



Rac-1



Meso-2



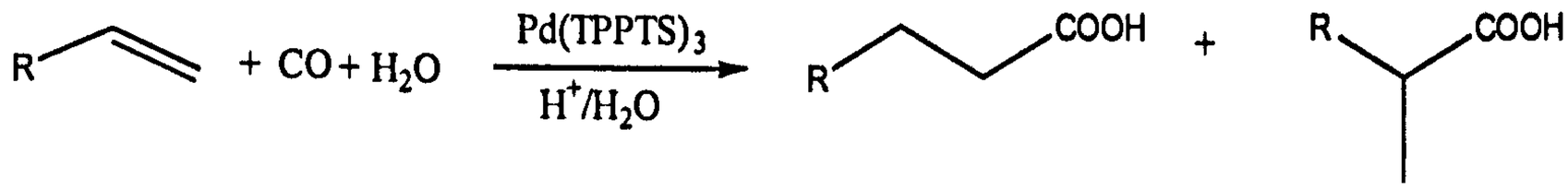
Rac-2

Scheme 2- 9: Structure of meso-1/ 2 and rac-1/ 2 ligands

If propene is the substrate, catalysts from meso-1 and rac-1 provide different activities and the same happens in the methoxycarbonylation of C_{11}/C_{12} olefins to linear C_{12}/C_{13} esters.

Van Leeuwen has recently reported the methoxycarbonylation of ethene catalysed by palladium complexes derived of 1,1'-bis(diphenylphosphino)ferrocene (dppf) and 1,1'-bis(diphenylphosphino)octamethylferrocene (dppomf).[13] Surprisingly, they perform very differently, since the former produces a variety of low molecular weight oxygenated compounds, whereas the latter produces methyl propanoate selectively.

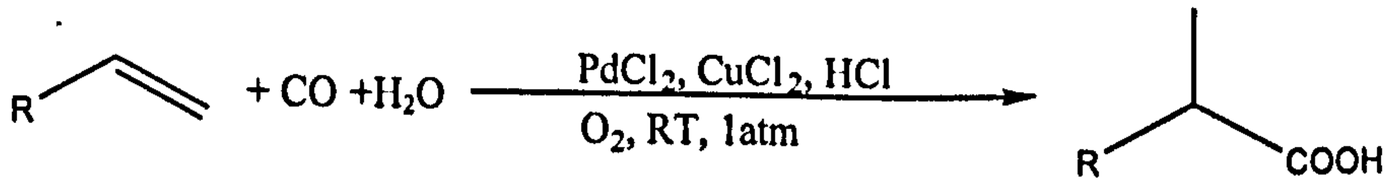
In order to make the separation of the homogeneous catalyst from products of hydrocarbonylation easier, Bertoux[38,44] has recently designed a system consisting of a water soluble palladium complex of trisulfonated triphenylphosphine (TPPTS) as catalyst and a Bronsted acid as promoter dissolved in an aqueous solution (*Scheme 2- 10*)



Scheme 2- 10: Hydrocarbonylation of alkenes with water soluble ligands

As a consequence of the low solubility in water shown by high α-alkenes, it is necessary to have mass transfer promoters like an alkali metal halide or a protective-colloid agent, such as polyvinylalcohol (PVA), in the catalytic phase, since the rate determining step is the mass transfer between aqueous and organic phases. This allows the catalyst to maintain its activity at high temperature (>100 °C) for more than 1 hour. By adding lithium chloride the catalyst maintains its activity even at 120°C. The highest activity was obtained when the LiCl/Pd molar ratio was 10: 20. Under these same conditions some other metal halides were tested. The most active were those containing Na^+ and K^+. The addition of 0.25 equivalents of PVA provided similar results to those obtained when 10 equivalents of LiCl were used. If the hydrocarbonylation mechanism is considered, catalyst deactivation occurs when palladium (0) species form agglomerates. The role of alkali metal halide and PVA is to prevent the colloid from agglomerating and allow it to react with CO to regenerate mononuclear Pd complexes.

Alper[45] also studied a catalyst system based in $PdCl_2$-$CuCl_2$ in the presence of HCl (*Scheme 2- 11*).



Scheme 2- 11: Hydrocarbonylation of alkenes under mild conditions

The role of the $CuCl_2$ is to reoxidise Pd^0 to Pd^{2+} (active species) by reduction of Cu^{2+} to Cu^0 and the role of the O_2 is to reoxidise the Cu^0 to Cu^{2+}. For the hydrocarboxylation of 4-methylstyrene the above system was used with the addition of PPh_3[46]. The amount of PPh_3 has little influence on the selectivity but it is important in increasing the speed of the reaction.

The role of the HCl in both systems is not very well known and there are two possible explanations: Cl^- acts as an anionic ligand or the acidity of the proton is important. Other acids were tested (HF, H_2SO_4) and there was a reduction in the conversion. This is why it is suggested that the presence of Cl^- is crucial.

Recently a patent by Drent[48] describes a process for the carbonylation of ethylenically unsaturated compounds using DTBPMB and a Pd $(OAc)_2$ as a source of cationic Pd^{II}. The unsaturated substrates have at least 3 carbon atoms although those having 4-14 are preferred and they can have substituents (alkyl and aryl groups containing heteroatoms) or not. The examples shown in the application are 1-octene, 2-octene and methyl-3-pentenoate. An acid is required in this system, with sulphonic acids being particulary preferred. The molar ratio of the source of anions and palladium used varies from 1: 1 to 5: 1.The application also specifies in the examples shown that an aprotic solvent must be used. Temperatures in the range of 50-250 ^{0}C and pressures in the range of 1-100 bar are claimed although all the examples shown are carried out at 100 ^{0}C and in the region 20-60 bar. The linear selectivity observed is 97.5-99 %.

2.2. Methoxycarbonylation of alkenes

The main focus of the research has been the methoxycarbonylation of 1-octene but other commercially interesting substrates have also been studied, such as 1-dodecene, 1-hexene, styrene, allyl alcohol, butadiene and pentenes. The commercial interest of these reactions is based on the potential uses of the esters formed as detergent, plasticisers and soaps.

The following sections show a detailed study using the standard catalytic solution described in the experimental section in chapter 7 [$(Pd_2(dba)_3$], DTBPMB, MSA and methanol] the effect of several reaction condition parameters have been examined.

2.2.1. Methoxycarbonylation of 1-octene.

2.2.1.1. Effect of DTBPMB concentration and DTBPMB: Pd ratio.

Carbonylation of 1-octene in methanol produces methyl nonanoate as linear product and 2-methyl octanoate as branched product, the former being the desired product (*Figure 2-1*).

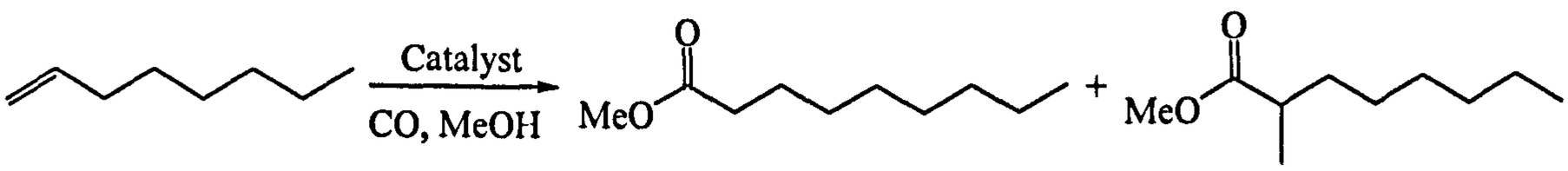


Figure 2-1: Methoxycarbonylation of 1-octene.

The ratio DTBPMB: Pd was raised from 1.5:1 to10: 1, whereas the temperature and the pressure remained constant at 80 °C and 30 bar of CO respectively. Table 2- 1 lists the experimental conditions used and the results obtained.

Table 2- 1: Effect of ligand: Pd ratio

[Pd] (M)	[L] (M)	1-oct (%)	Isom (%)	l (%)	b (%)	Conv (%)	Sel (%)	l: b
0.008	0.0800	0	7.0	87.2	6.4	93.4	93.4	15
0.008	0.0400	0.04	0	94.3	5.7	>99.9	94.3	16
0.008	0.0250	0.08	8.4	86.1	5.3	91.5	94.0	16
0.008	0.0125	1.1	53.9	43.8	1.2	45.0	97.4	38

P= 30 bar, T= 80 °C, t= 3 h, [MSA]= 0.08M

1-oct: 1-octene; isom: isomerised alkenes; conv: conversion; sel: selectivity.

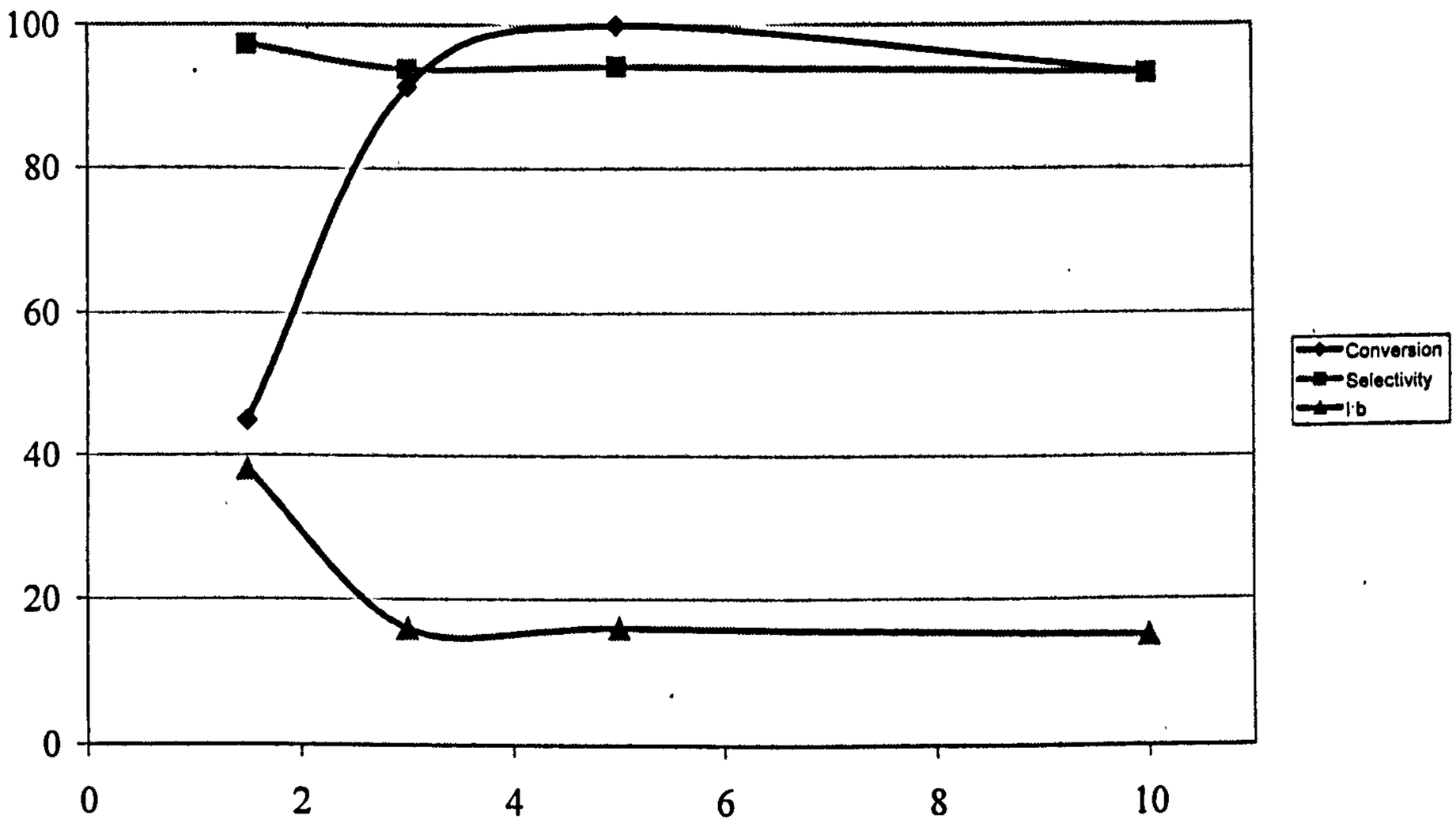


Figure 2- 2: Graph showing the effect of ligand concentration.

The recovered alkenes had isomerised to a thermodynamic mixture of 2-cis and trans, 3-cis and trans and 4-cis and trans octenes. Only 5 % of this mixture was 1-octene. The conversion to esters increased with DTBPMB: Pd, reaching a maximum at DTBPMB: Pd= 5:1 and decaying at higher ratios, whereas the selectivity to linear ester was not greatly affected, although it slightly increased at lower ligand concentration. It is noteworthy that when the ratios were 1.5:1 and 3:1 fast catalyst decomposition occurred to yield metallic palladium. If DTBPMB: Pd= 5:1 or 10:1, the palladium black formation was completely

suppressed, suggesting that a larger excess of phosphine in the reaction medium forces the coordination of the ligand to the metal centre. Thus, the most effective performance of the catalyst was provided by a Pd: DTBPMB= 1:5 and this ratio was used throughout the study (*Figure 2- 2*).

2.2.1.2. Effect of solvent system and protic solvents.

The methoxycarbonylation of 1-octene had been previously reported to give high conversion and selectivity in the presence of an aprotic solvent.[22] Very suitable aprotic solvents are those having a dielectric constant in the range of 3 to 8, at 298.15 K and 1 bar, like anisole (4.3), diethyl ether (4.3), methylpentanoate (5.0), diphenylether (3.7), dimethyl adipate (6.8), tetrahydrofuran (7.5), methylnonanoate (3.9). Anisole is the preferred solvent.

If a mixture of a non polar solvent like toluene (dielectric constant of 2.4) and methanol (dielectric constant of 33) was used, the selectivity and l: b ratio observed were very high (96.3 % and 28:1, respectively); not so the conversion (82 %). An additional problem was the measurement of the kinetics, since both [1-octene] and [MeOH] varied during the course of the reaction, it was not first order. This problem was overcome by the use of methanol without a cosolvent. Doing so, the conversion increased significantly although selectivity and l: b ratio decreased slightly. Thus, the presence of an aprotic solvent (low dielectric constant) did not improve the performance of the catalyst, since methanol itself gave the most satisfactory results.

A wide range of alkyl nonanoates could be synthesised by using alcohols other than methanol as a solvent. The following alcohols were employed either as a

pure solvent or in a co-solvent mixture: EtOH, ^{t}BuOH, THF+ triethyleneglycol, THF+ ethyleneglycol, ^{t}BuOH + glycerol.

Table 2- 2 and *Figure 2- 3* shows the results obtained in each case.

Table 2- 2: Effect of solvent system and protic solvents

Solvent system	[Alc] (M)	1-oct (%)	Isom (%)	l (%)	b (%)	Conv (%)	Sel (%)	l: b
Toluene/ MeOH	3.8	0.2	17.7	79.3	2.8	82.1	96.9	28
THF/ Ethgly	2.7	0	0	95.8	4.2	100	95.8	22.8
THF/ Triethgly	3.1	0	1.2	98.3	1.7	98.8	99.5	57.8
MeOH	20.6	0.04	0	94.3	5.7	99.96	94.3	16.5
EtOH	13.9	0	0	96	4.7	100	98.4	15.7

[Pd]=0.008M, [L]=0.04M, [MSA]=0.08M, [S]=1.3M, t=3h, P= 30 bar, T= 80°C.

The reactions in EtOH and in THF/ ethyleneglycol went to completion after 3 hours, reaching higher selectivity and l: b ratio than in MeOH. In THF/ triethyleneglycol the conversion was slightly lower although selectivity and l: b ratio were the highest observed. This is a particularly interesting reaction as it leads directly to an ethoxylated detergent molecule with very high selectivity. The higher conversion observed in EtOH and THF/ ethyleneglycol is attributed to the higher nucleophilicity of ethoxide and ethyleneglycoxide compared to methoxide, suggesting that the alcohol is involved in the rate determining step of the reaction. Likewise, the higher selectivity obtained is ascribed to the higher steric bulk of those two alkoxides compared to methoxide, since the nucleophilic attack to the branched palladium-acyl intermediate will be highly hindered, forcing the formation of the linear ester (section 2.2.7). However, when ^{t}BuOH was used, no reaction occurred despite its highly nucleophilic character. The steric effects appear to be more important than the electronic effects in this case. This finding led us to the use of ^{t}BuOH as a co-solvent mixture with glycerol. The ratio 1-octene: glycerol was changed from 3:1 to 1:2 in order to form the

mono, di and triester. In all cases, the product obtained contains two alkene chains, one in each terminal alcohol. Unfortunately, when using a 3: 1 ratio 1-octene and glycerol are no longer miscible and the reaction cannot proceed.

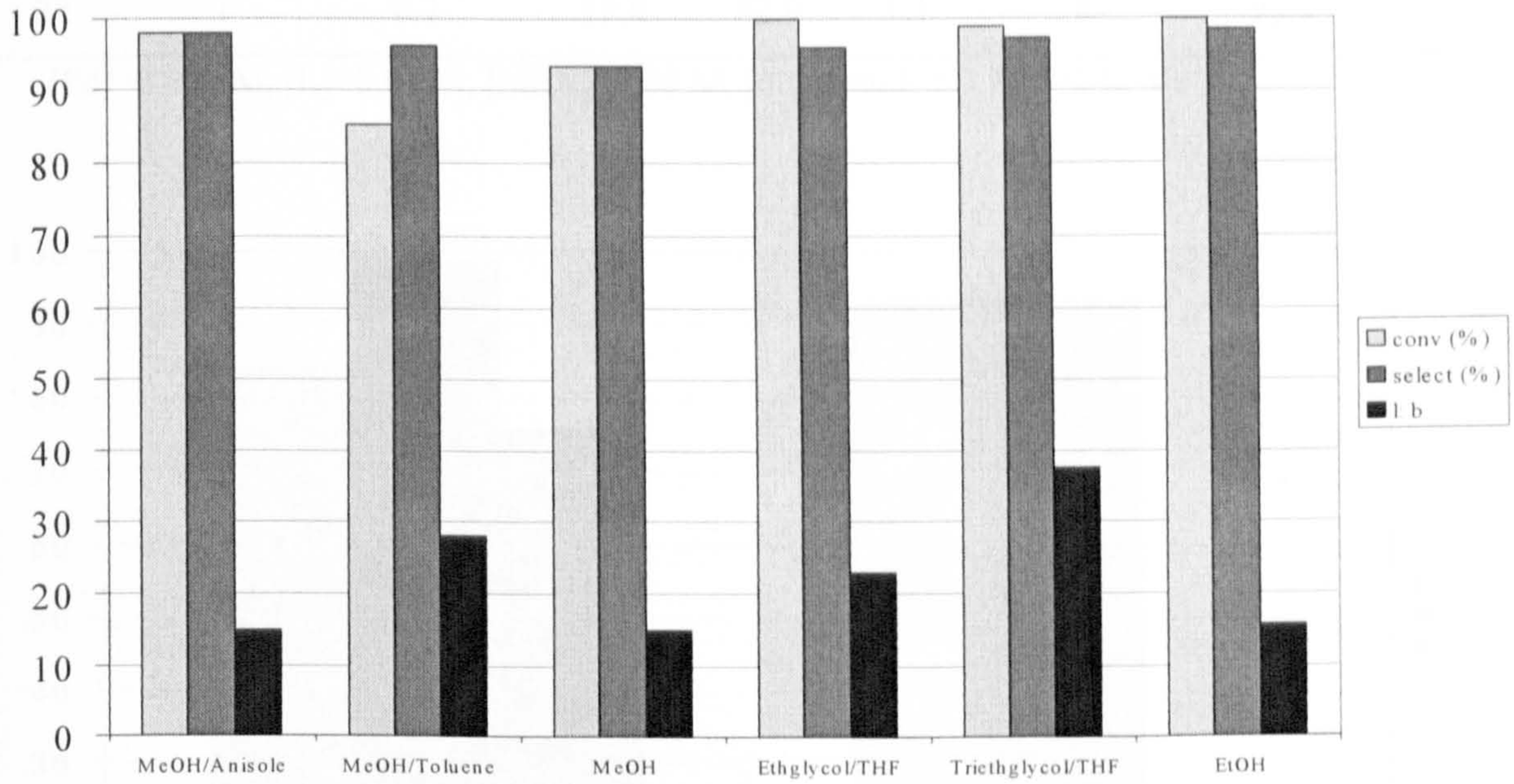


Figure 2- 3: Graph showing the effect of different solvent systems

2.2.1.3. Effect of pressure and temperature.

As part of a mechanistic study 1-octene was stirred with the catalyst in MeOH at room temperature and under 1 bar CO. It was found that after 3 hours not only was the conversion quite high (84%) but also the selectivity (98.7%) and the l:b ratio (75.9:1) were higher than when more severe conditions were used. In view of this result a more detailed study of methoxycarbonylation of 1-octene under different temperature and pressure conditions was carried out. Table 2- 3 and *Figure 2- 4* show the reaction conditions and the results obtained.

Table 2- 3: Effect of pressure and temperature

T (°C)	P (bar)	l-oct (%)	Isom (%)	l (%)	b (%)	Conv (%)	Sel (%)	l: b
80	30	0.04	0	94.3	5.7	>99.9	94.3	16.5
40	1	0.3	25	72.5	2.2	74.7	97	34.1
RT	30	0.4	49	49.2	0.9	50	98.5	54.7
RT	1	0.2	15.8	82.9	1.1	84	98.7	75.9

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M, [Substrate]=1.3 M, t=3 h, MeOH

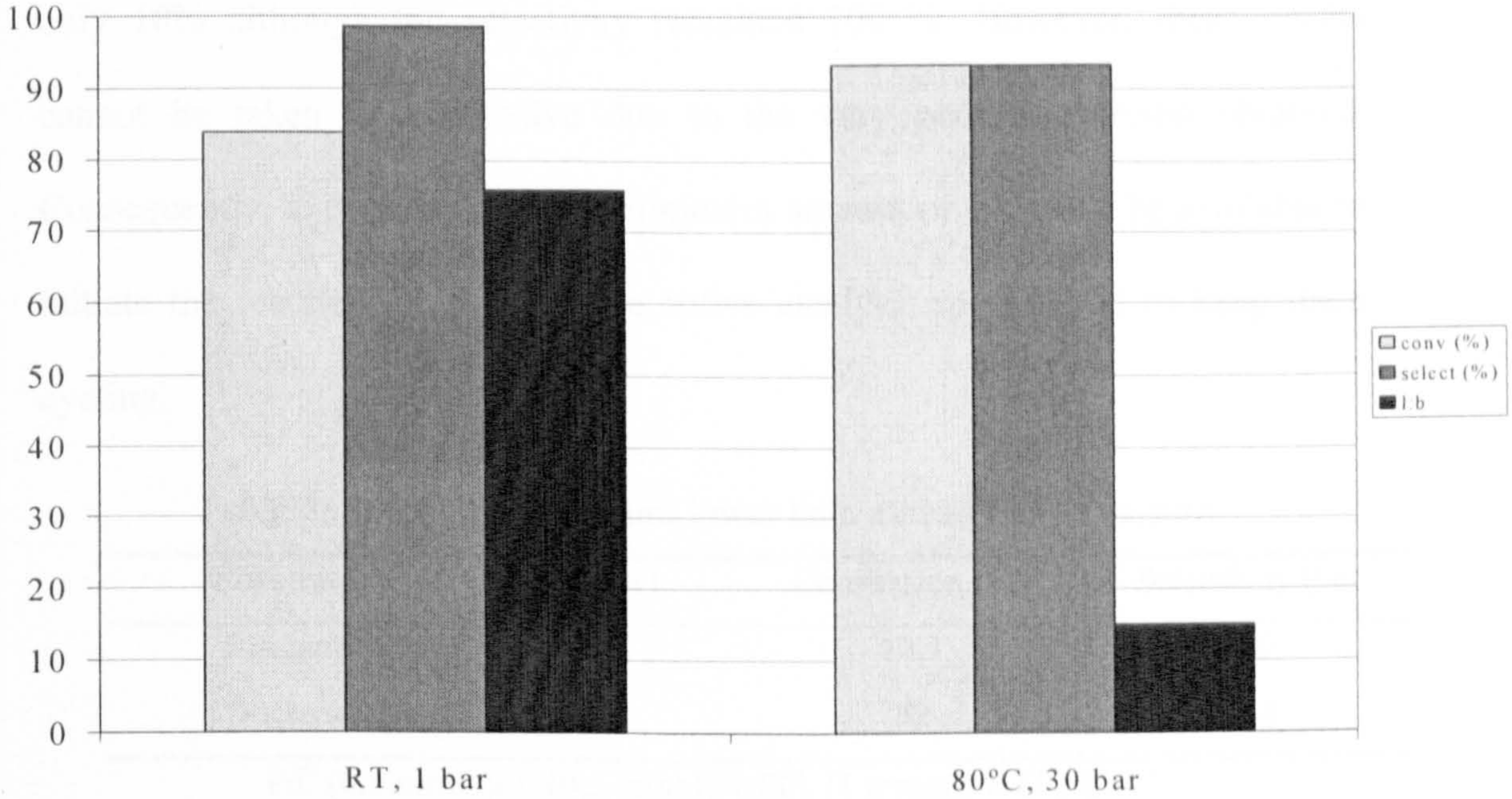


Figure 2- 4: Graph showing the comparison of different conditions of pressure and temperature for carbonylation of 1-octene.

The high conversion achieved when CO was bubbled through the solution could be attributed to the evaporation of the substrate. For this reason the reaction was carried out in a closed vessel at room temperature under 4 bar of CO. Under these conditions 82 % conversion and 98.6 % selectivity were achieved. These results suggest that high pressure is not required to get high conversion and is detrimental to selectivity, thus prompting us to investigate the effectiveness of this catalytic system at a pressure lower than atmospheric pressure. The pressure

chosen to carry out the present study was 0.2 bar, which was obtained by mixing CO and N_2 in a ratio of 1: 4 at a total pressure of 1 bar, so that only 20% of the mixture is CO. The results of these reactions are shown in Table 2- 4. A lower pressure than atmospheric pressure did not have the expected effects. On the basis of a faster reaction at 1 bar of CO than at 30, it was expected to be faster under 0.2 bar than under 1 bar. Surprisingly, after 3 hours the conversion was only 10% although the selectivity remained 100 %. However, these results cannot be taken as conclusive due to the very poor conversion obtained. Consequently, it is believed that a minimum amount of CO must be available to initiate the reaction by forming the active catalytic species and to keep them cycling.

Table 2- 4: Effect of pressure lower than atmospheric pressure

Substrate	P (bar)	Conversion (%)	Selectivity (%)
1-octene	0.2	10.3	100
1-octene	4	82	98.6

Pd^0 (0.1 mmol)/ L (0.5 mmol)/ MSA (1 mmol)/ RT/ 3 h.

2.2.1.4. Comparison of different palladium precursors.

We were also interested in knowing if $Pd_2(dba)_3$ was the most effective palladium precursor among all the available palladium precursor that could be employed. For this reason other common palladium compounds, like $PdCl_2$ and $Pd(OAc)_2$, were investigated. The results obtained are shown in the Table 2-5.

At low temperature palladium chloride turns out to be more active than $Pd_2(dba)_3$, in contrast to what happens at high temperature. Surprisingly, $Pd(OAc)_2$, which is the most often used palladium precursor, showed no activity when combined with DTBPMB due to *ortho*- metallation of the ring.[19] The

preformed catalyst [$PdCl_2$(DTBPMB)] was also tested. It was expected to be more active than the non preformed complex since the ligand is already coordinated to the metal. However, it did not show high catalytic activity and after 3 hours the catalyst decomposed completely into palladium black. It must be noted that no excess of ligand was added to the preformed catalyst and therefore the Pd: DTBPMB ratio is lower than in the rest of examples.

Table 2- 5: Different palladium precursors tested.

Pd precursor	Pd: ligand	T (°C)	P (bar)	Conversion (%)	Selectivity (%)
$Pd_2(dba)_3$	1: 5	50	30	90	96
$Pd_2(dba)_3$	1: 5	80	30	99.9	94.3
$PdCl_2$	1: 5	50	30	92	97
$PdCl_2$	1: 5	80	30	97	93
$PdCl_2$(DTBPMB)$^{(*)}$	1: 1	80	30	34	95.5
$Pd(OAc)_2$	1: 5	80	30	0	0

(*): [Pd]= 1.5 x 10^{-3} M, t= 16 h

2.2.1.5. Four isomers of octene.

It was previously shown that the starting material, 1-octene, isomerised significantly after short reaction times. When the isomerisation equilibrium is established only less than 5 % of the initial 1-octene remains. Nevertheless excellent linear selectivity was obtained throughout the reaction. Therefore, this catalytic system should be capable of maintaining the equilibrium established between the internal and terminal alkenes to produce linear esters. Therefore, reactions using 2-, 3- and 4-octene as the substrate were carried out. For 3- and 4-octene the reaction time was longer than for 1-and 2-octene assuring the reaction would proceed to completion. Table 2- 6 shows the conditions used and the results obtained.

Table 2- 6: Different isomers of octene

Substrate	t (h)	l-oct (%)	Isom (%)	l (%)	b (%)	Conv (%)	Sel (%)	l: b
1-octene	3	0.04	0	94.3	5.7	>99.9	94.3	16
2-octene	3	0.1	4.8	89	6.1	95.6	97.1	14.8
3-octene	17	0	0	93.9	6.1	99.6	94	15
4-octene	17	0	0	94	6	100	93.9	15.6

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M, [S]=1.3 M, P=30 bar, T=80 °C

For the four substrates the selectivity to methyl nonanoate and the l: b ratio are similar (~93% and ~15: 1). This proves that isomerisation of the alkenes occurs during the catalytic cycle and that the terminal alkene is preferentially carbonylated (*Figure 2- 5*). The isomerisation process will be discussed in section 2.2.3.

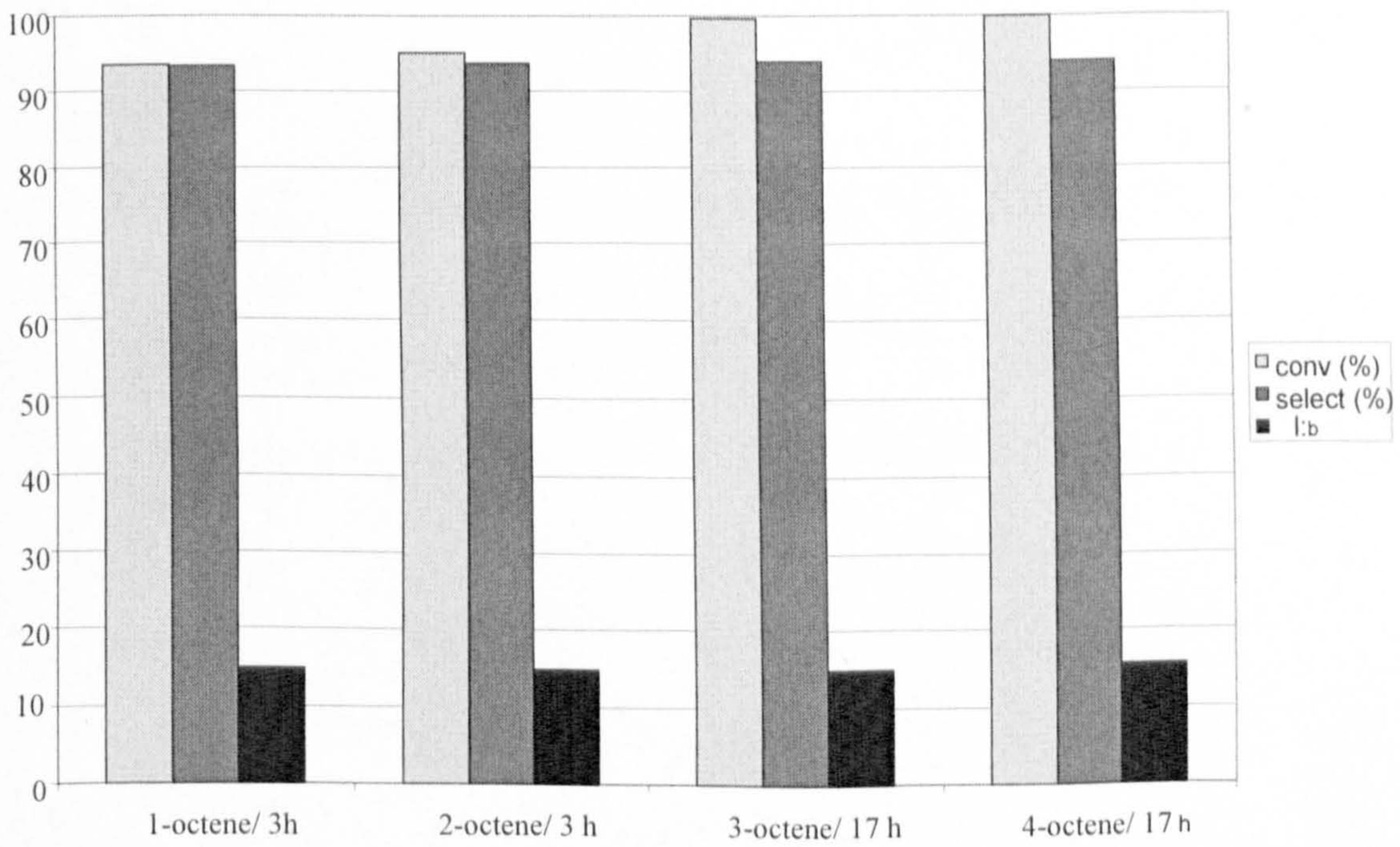


Figure 2- 5: Graph showing the comparison of different octenes.

2.2.2. Other substrates.

In order to test the generality of the reaction the selective formation of longer methyl esters was attempted. It was found that the same system catalysed the

carbonylation of other longer alkenes under the same conditions to yield the corresponding methyl esters. In the light of these observations some research on methoxycarbonylation of unsaturated carboxylic acids and derivatives in addition to unsaturated fatty esters has been carried out. Dienes were also studied, especially 1, 3-butadiene due to the great industrial importance of dimethyl adipate and 3-methyl pentenoate, which are intermediates in the synthesis of nylon. The methoxycarbonylation of substrates containing allyl groups, traditionally a difficult reaction, was also attempted. When using allyl alcohol as the substrate, methyl 3-hydroxy-2-methylpropanoate (which is an intermediate in the synthesis of methyl methacrylate) was the desired product. Styrene has also been tested since it is used as the starting material in the synthesis of anti-inflammatory agents[15], so in this case the desired product was the branched ester instead of the linear.

2.2.2.1. Terminal alkenes other than 1-octene.

An analogous study has been carried out with 1-hexene. The products expected are shown in *Figure 2- 6*. Table 2- 7 shows the conditions used and the results obtained.

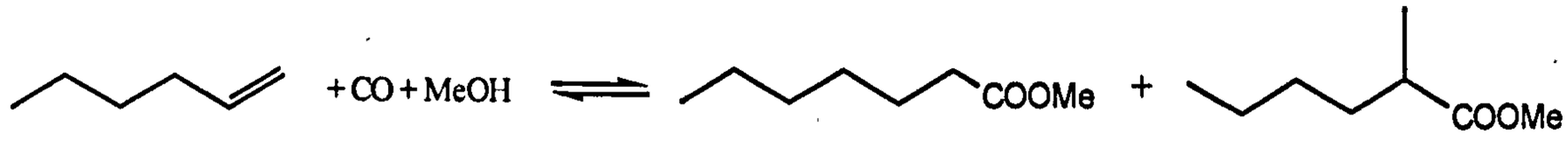


Figure 2- 6: Methoxycarbonylation of 1-hexene

Table 2- 7: Effect of pressure and temperature

P (bar)	T (°C)	1-hex (%)	Isom (%)	l (%)	b (%)	Conv (%)	Sel (%)
1	RT	0	0	100	0	100	100
1	10	0	0	100	0	100	100
1	0	0	0	100	0	100	100
3	RT	0	0	100	0	100	100
0.2	RT	0	0	100	0	100	100

[Pd]=0.008M, [L]=0.04M, [MSA]=0.08M, t=3h

Being a shorter chain alkene getting higher conversions than those obtained with 1-octene was expected. Surprisingly, independently of the reaction temperature the reaction was always complete after 3 hours, the linear ester (methyl heptanoate) being the only product observed. Due to the small pocket angle of the ligand, coordination of the less bulky 1-hexene to the metal centre is favoured and the reaction proceeds faster than for largely sterically hindered substrates, like 1-octene. No matter the reaction pressure (0.2, 1, 3 bar), the only product recovered at the end of the reaction was methyl heptanoate. The methoxycarbonylation of 1-dodecene was also studied.

Figure 2- 7 shows the products expected from this reaction:

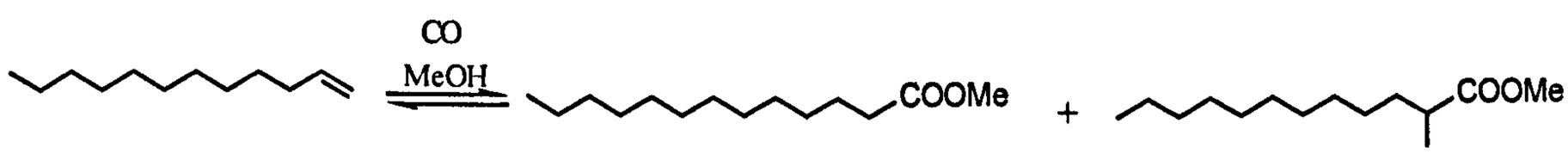


Figure 2- 7: Methoxycarbonylation of 1-dodecene

Due to the longer length of the chain, methoxycarbonylation of 1-dodecene was expected to be slower than all alkenes previously described. Table 2- 8 shows the conditions used and the results obtained.

Table 2- 8: Effect of pressure and temperature

P (bar)	T (°C)	1-dod (%)	Isom (%)	l (%)	b (%)	Conv (%)	Selec (%)
30	80	0	0	90.9	9.1	100	99.98
30	RT	10.3	56.7	32.3	0.7	33	98
3	80	1	0	93.7	5.2	99	95
3	RT	1.1	27.9	69	2	71	98.7
1	RT	12.8	56.9	29.8	0.5	30.3	98
1	10	86.1	8.2	5.4	0.3	18	99
1	0	15.1	66.5	18.2	0.2	18	99

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M, t=3 h

When severe conditions of pressure and temperature were used, the reaction was complete after 3 hours but the selectivity achieved was only 90.9 %. Reducing the temperature to 25 °C, the conversion dropped dramatically (33 %) but the selectivity increased to 98 % despite the high isomerisation. If the pressure was reduced to 3 bar but the temperature remained 80 °C, the conversion was unaffected (99 %) and 95 % selectivity was achieved. Lowering the pressure to 0.2 bar led to a dramatic drop in the conversion (9.2 %), the selectivity remaining 95 %. If under 3 bar of CO the temperature was then reduced to 25 °C the conversion dropped to 71 % but the selectivity increased to 98 %. Further reduction of the temperature did improve the selectivity but the conversion decreased to <20 %. These observations led us to conclude that (1) low temperature reduces the reaction rate and (2) low pressure and low temperature very much favour the formation of the linear palladium-acyl intermediate which lead to the linear ester. A possible reason for this is discussed in section 2.2.7.

Given the conversion and selectivity observed for 1-dodecene, a longer chain alkene, 1-octadecene, was studied. Very little conversion (5.7 %) and 100 %

selectivity to the linear ester were obtained after 3 hours at 80 °C under 30 bar of CO. In this case the steric bulk of the alkene clearly inhibits the reaction.

It was interesting to study the behaviour of alkenes which combine two aspects, already studied separately, such as branches and internal double bonds. Among all the branched alkenes which keep these two conditions, branched pentenes looked to be the most appropriate for this purpose. Thus, the esters obtained could be formed by direct methoxycarbonylation or by tandem isomerisation-methoxycarbonylation (*Figure 2- 8* and Table 2-9)

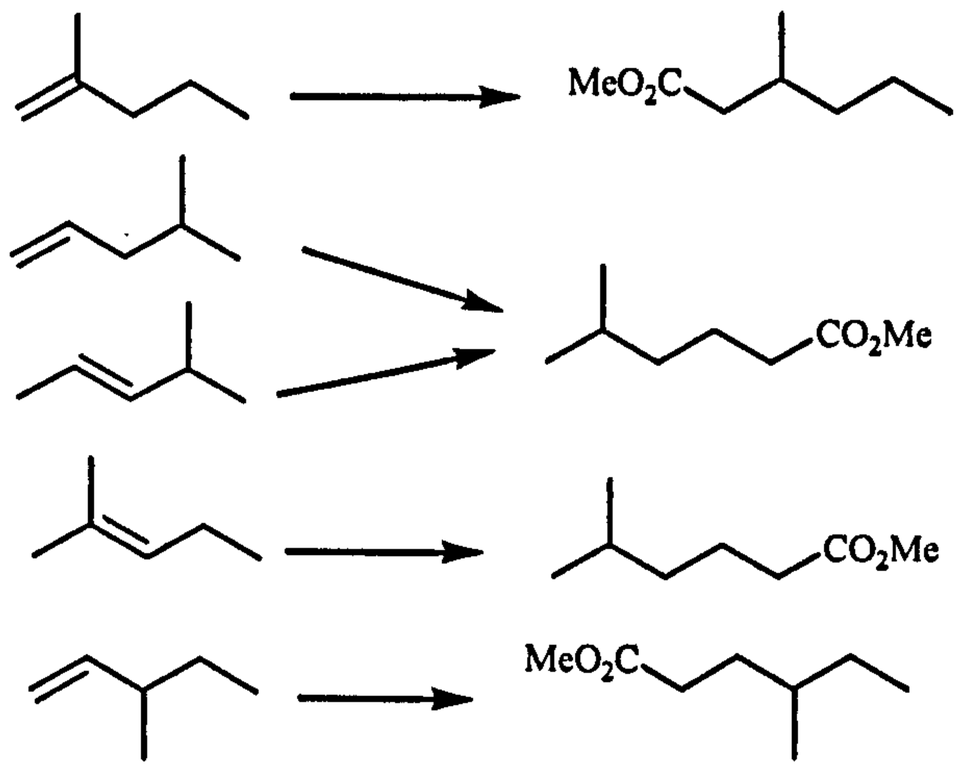


Figure 2- 8: Methoxycarbonylation of branched pentenes

Table 2- 9: Different branched pentenes

Substrate	5-MMH	3-MMH	4-MMH	Conv (%)	Selec* (%)
2-methyl-1-pentene[1]	96	4	0	100	96
3-methyl-1-pentene[1]	0	0	100	100	100
4-methyl-1-pentene[1]	99.4	0.6	0	100	99.4
2-methyl-1-pentene[2]	20	80	0	100	80
2-methyl-2-pentene[2]	97	3	0	100	97
4-methyl-2-pentene[2]	100	0	0	100	100

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M, P=1 bar, RT, t=3 h
(1): passing CO. (2): bubbling CO. (*): Selectivity to carbonylation in position one.

Independently of the initial pentene, the reaction went to completion in 3 hours.

Terminal pentenes, like 2-methyl-1-pentene, 4-methyl-1-pentene and 3-methyl-1-

pentene, were carbonylated in position 1 selectively, giving the correspondent ester, methyl 5-methyl-hexanoate in the former two cases and methyl 3-methyl-hexanoate in the latter case. Having an internal pentene, like 4-methyl-2-pentene, as starting material has no influence on the ester formed, since the product obtained corresponds to the carbonylation of position 1 to afford methyl 5-methyl-hexanoate. This is in agreement with results obtained with internal octenes, in which the terminal position was preferentially carbonylated. Interestingly, for 2-methyl-1-pentene, the product depended upon the availability of CO (*Figure 2- 9*). Thus, when CO was bubbled through the solution, the major product (96 %) was methyl 3-methylhexanoate (little double bond isomerisation had occurred) whilst if CO was passed over the stirred solution, the major product was methyl 5-methylhexanoate (the double bond had isomerised past the branching point and the least hindered terminal metal alkyl was trapped preferentially).

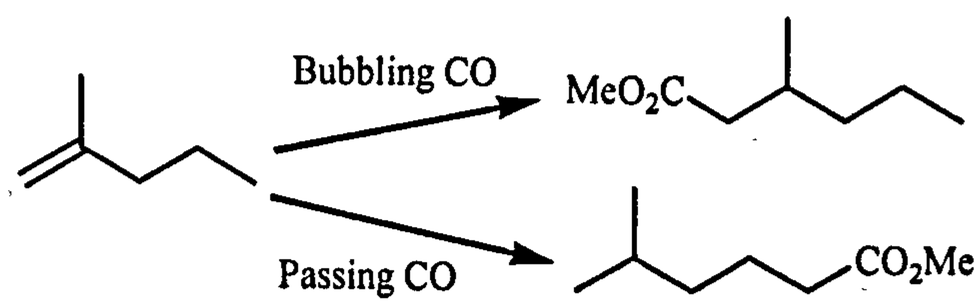


Figure 2- 9: Methoxycarbonylation of 2-methyl-1-pentene under different conditions

Using styrene as the substrate, methoxycarbonylation and hydrocarboxylation were carried out. In order to synthesise the carboxylic acid rather than the ester, THF was chosen as the cosolvent of water. *Figure 2- 10* illustrates the products obtained when MeOH was used.

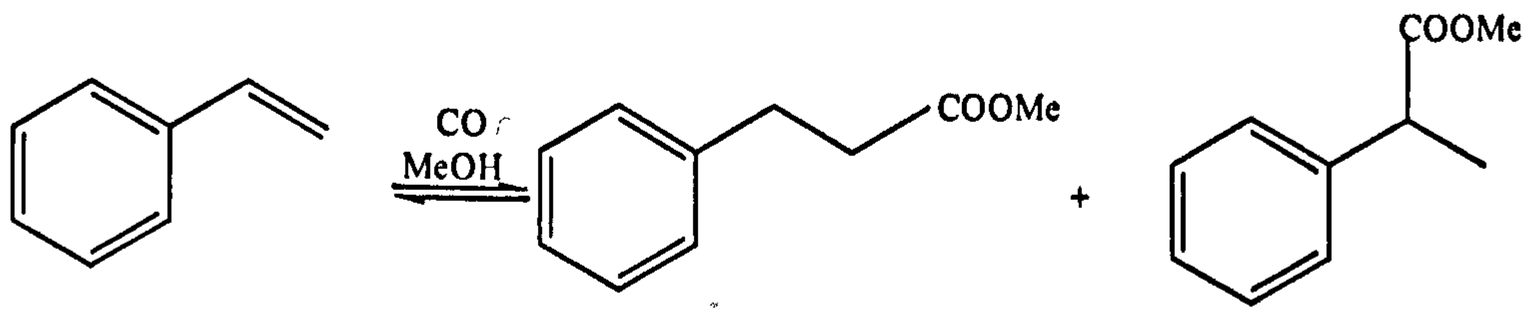


Figure 2- 10: Styrene methoxycarbonylation

Either in water or in MeOH the reaction was complete after 3 hours achieving selectivities of 70.7 % and 73.1 %, respectively, with very similar l: b ratio 2.4: 1 and 2.8: 1, respectively. The branched product is the desired one from the carbonylation of styrene either in water or in an alcohol in order to produce carboxylic acids or esters. The increased amounts of linear product obtained when using DTBPMB provide further evidence of the strong linear directing properties of this particular system.

2.2.2.2. Acrylates.

Acrylates were the substrates chosen to explore the effect of the presence of a functional group in an unsaturated chain. The presence of a functional group in the alkene might change the reactivity of the double bond and therefore the coordination to the metal centre might not be the same. If this functional group is electron withdrawing, the double bond will be poorer in electrons than that in a non-functionalised alkene, favouring the binding to the metal and therefore favouring the carbonylation reaction.

In addition, in this sort of substrate there are two conjugated double bonds, C=C and C=O, present. As known, conjugated double bonds are very stable; consequently, these compounds are less reactive than those which have non-conjugated double bonds.[14] Thus, the high stability of exhibited by this compounds may inhibit the methoxycarbonylation.

The methoxycarbonylation of methyl acrylate, which is a linear three carbon chain compound, and methyl methacrylate, which is a branched four carbon chain compound, were investigated. As a first attempt the reaction was carried out at room temperature and under 1 bar of CO. The expected products are shown in *Figure 2- 11*.

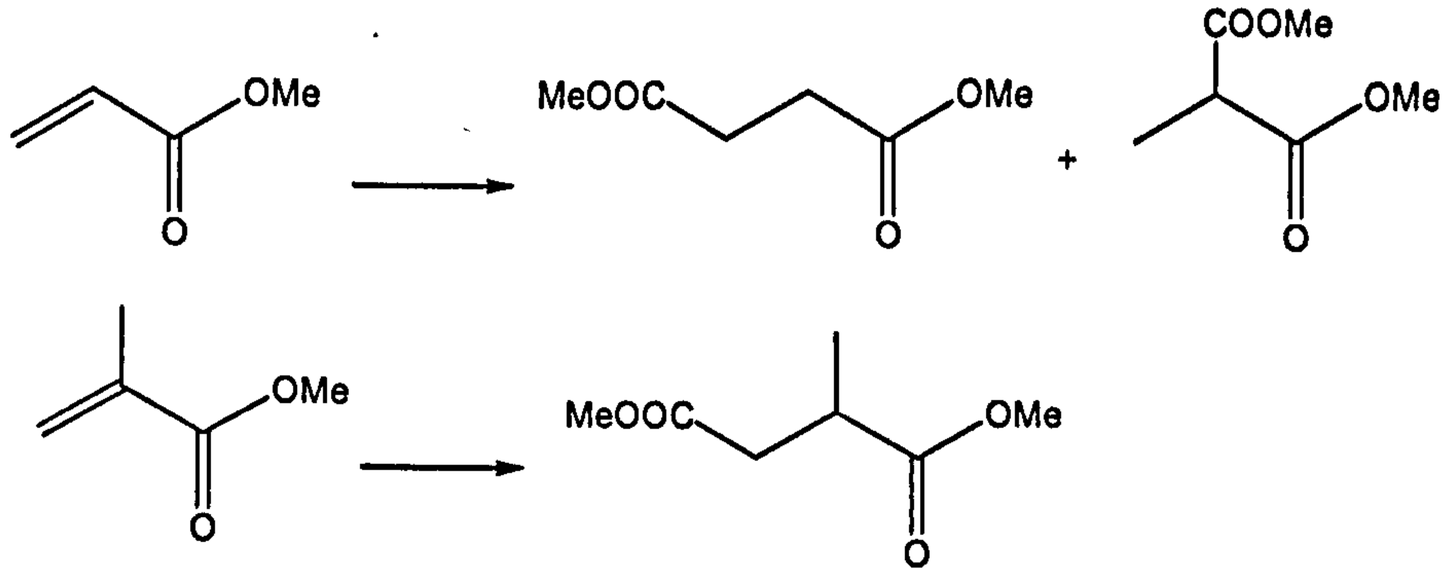


Figure 2- 11: Methoxycarbonylation of methyl acrylate and methyl methacrylate.

Under these conditions no reaction took place. It may be that the activation energy is increased because of the need to break the conjugation. Therefore, the reaction was effected at 40°C and 20 bar. Methoxycarbonylation of both methyl acrylate and methyl methacrylate occurred smoothly to produce the corresponding linear esters in 77% and 100% yield, respectively. In the case of methyl acrylate, a side-reaction resulting from methanol addition to the double bond with formation of a 23 % yield of 3-methoxy-methylpropanoate took place (Table 2- 10).

Table 2- 10: Methoxycarbonylation of methyl acrylates.

Substrate	Conversion (%)	Selectivity (%)
Methyl acrylate(*)	100	77
Methyl methacrylate	100	100

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M, P=20 bar, 40 °C, t=3 h
(*): 23% of 3-methoxy-methylpropanoate was also found. 77% of the total amount of esters were linear

As far as we are aware, there are not many reports on the catalytic formation of asymmetric esters despite being a reaction of great importance. Methoxycarbonylation of butyl acrylates will give unsymmetric esters assuming that no transesterification occurs (*Figure 2- 12*). The results obtained are shown in Table 2-11.

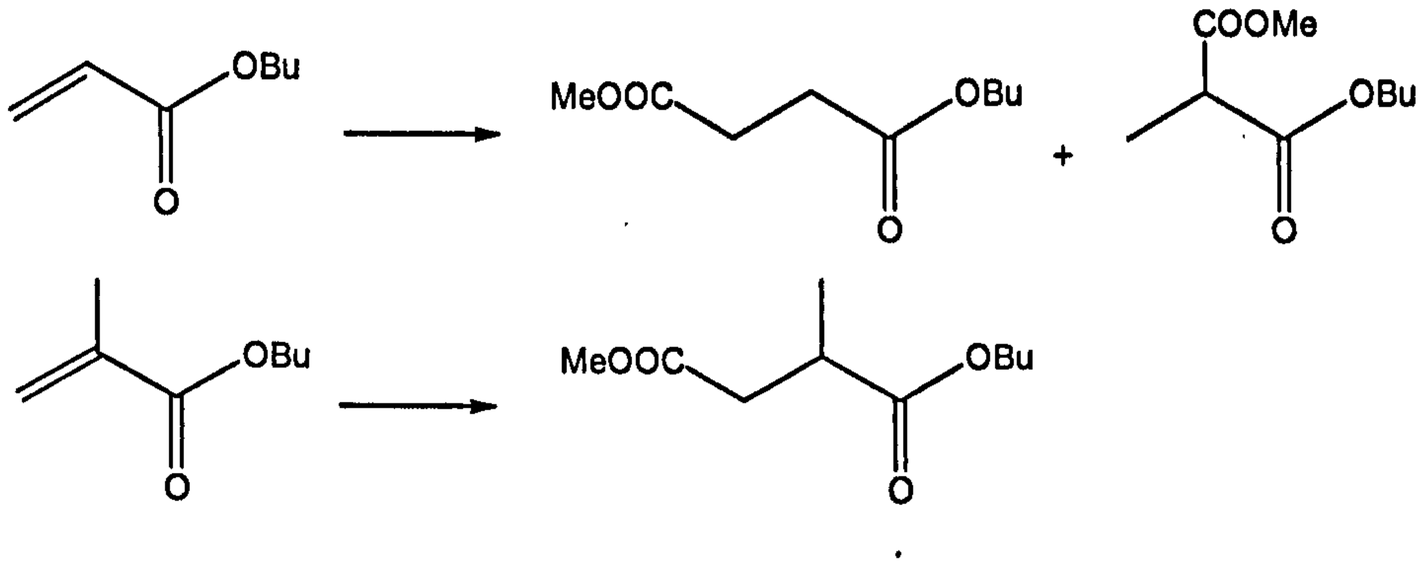


Figure 2- 12: Formation of unsymmetric esters from butyl acrylates.

Based on the results observed for methyl acrylate under the same conditions, low conversion of butyl acrylate was expected. Nonetheless, at 50 °C under 20 bar CO the reaction proceeded to completion affording the desired product in 95 % yield. The reaction of butyl methacrylate at 50 °C under 20 bar CO was next examined.

Table 2- 11: Methoxycarbonylation of butyl acrylates

Substrate	P (bar)	T (°C)	Conversion (%)	Selectivity (%)
Butyl acrylate	1	rt	32	71
Butyl acrylate	20	50	100	95
Butyl methacrylate(*)	20	50	100	93.4

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M
(*): 6.6% of 3-methyl-1,5-dimethylpentanoate was formed.

The target asymmetric ester was produced in 93.4 % yield. However, in this case, transesterification (nucleophilic substitution of butoxy by methoxy) occurred leading to the symmetric ester, 2-methyl-dimethylbutanedioate, in 6.6 % yield.

2.2.2.3. Unsaturated carboxylic acids.

Dimethyl adipate can be formed catalytically by methoxycarbonylation of butadiene, which being a gas is more difficult to manipulate, requiring special equipment. This prompted us to investigate an alternative system to produce dimethyl adipate.

Knowing that our catalyst is capable of converting a wide variety of internal and terminal alkenes and acrylates to the corresponding linear ester, methoxycarbonylation of unsaturated carboxylic acids and their derivatives, were studied (Table 2- 12).

Methoxycarbonylation of 3-methylpentenoate represents a straightforward method of producing dimethyl adipate. Isomerisation of the double bond to the terminal position rather than to the conjugated one is required for this purpose. Methoxycarbonylation-esterification of either 2-pentenoic acid and 4-pentenoic acid is required to produce dimethyl adipate. The former does not only have an internal double bond, which is known to be more difficult to carbonylate, but in addition, the internal double bond is conjugated with the carbonyl group, making the molecule more stable and unreactive. The latter has a terminal double bond, which tends to isomerise to give the more stable conjugated product 2-pentenoic acid. The case of 2-pentenenitrile is similar to that of 2-pentenoic acid, since the double bond is conjugated to the nitrile group. Methoxycarbonylation of 2-pentenenitrile will give 5-cyano-1-methylpentenoate, which is industrially used in the production of nylon. Methoxycarbonylation of 2-pentenoic acid and 4-pentenoic acid was carried out at 50 °C under 25 bar CO. The desired dimethyl adipate was produced in 97.5 % and 96.3 % yield, respectively. Reaction of

methyl-3-pentenoate performed at 50 °C under 20 bar CO gave dimethyl adipate in 99 % yield. In the three cases the reaction was complete after 3 hours.

The expected product coming from the esterification-methoxycarbonylation of 3-hexenoic acid is not as commercially attractive as dimethyl adipate, but it was interesting for us to see the effect of making the chain longer keeping the double bond in an internal non-conjugated position. The only product formed arose from methoxycarbonylation of the terminal carbon atom, affording heptanedioic dimethyl ester in 17.3 % yield. At first glance, there are some disadvantages in the use of these compounds. However, in spite of them the reactions were carried out under mild conditions of temperature and pressure, although more severe than the ones used for terminal alkenes. The presence of electron withdrawing groups in the unsaturated chain promotes the carbonylation reaction, keeping high selectivity to linear.

The presence of either electron withdrawing groups or conjugated double bonds in the chain did not make any difference either to the reactivity of the double bond or to the selectivity to the linear ester. This suggests that isomerisation to the terminal position followed by carbonylation is favoured and only terminal alkyl intermediates are carbonylated.

Since long chain unsaturated esters can be carbonylated, an attempt of carbonylating fatty acid esters where the double bond is burried deep in the chain was made. When methyl oleate, methyl linoleate and methyl linolenate were used as substrate the reaction was carried out at 80 °C and 30 bar. Methyl oleate gave high conversion (90-95 %) to afford the product arisen from the carbonylation in the terminal position. One of the two double bonds of methyl linoleate underwent methoxycarbonylation. However, the other double bond

remained although the exact position could not be detected. No reaction took place when methyl linolenate was the substrate.

Table 2- 12: Methoxycarbonylation of unsaturated carboxylic acids and derivatives.

Substrate	P(bar)	T(°C)	t(h)	Conv (%)	Select (%)
Methyl-3-pentenoate[1]	20	50	3	100	99
2-pentenenitrile[2]	1	Rt	3	32	100
2-pentenoic acid[3]	25	50	4	100	97.5
4-pentenoic acid[4]	25	50	4	100	96.3
3-hexenoic acid[5]	1	Rt	3	17.3	100

[Pd]=0.008 M, [L]=0.04 M, [MSA]=0.08 M
1. 3-methylpentenoate (21 mmol), 2. 2-pentenenitrile (21 mmol), 3. 2-pentenoic acid (9.9 mmol), 4. 4-pentenoic acid (9.1 mmol), 5. 3-hexenoic acid (17 mmol).

2.2.2.4. Substrates containing allyl groups.

Among these compounds allyl alcohol is the most attractive commercially since dehydration of the branched methyl ester would lead to the formation of methyl methacrylate. *Figure 2- 13* shows the expected products from allyl alcohol as the substrate.

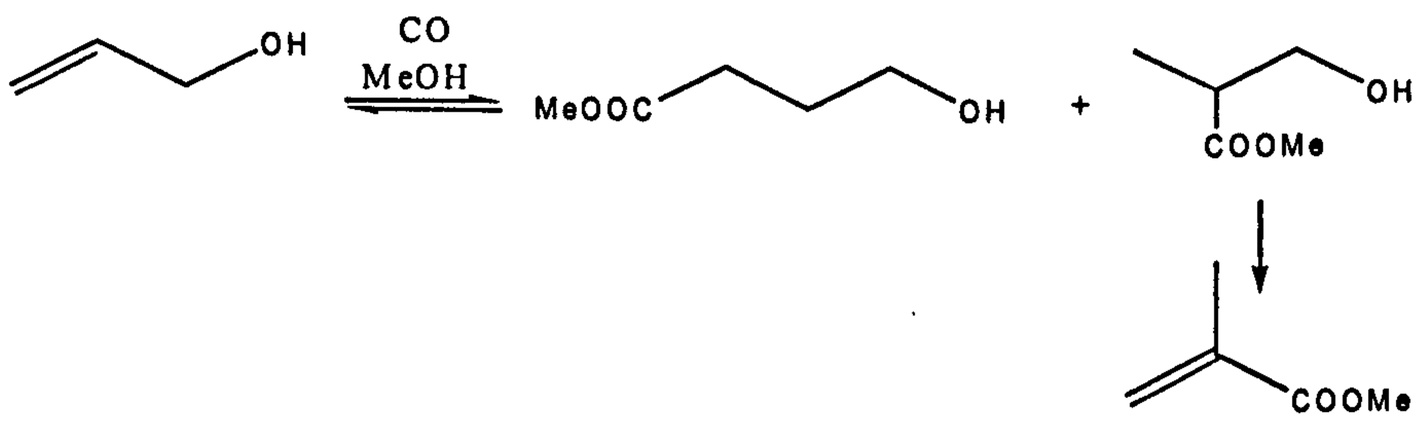


Figure 2- 13: Methoxycarbonylation of allyl alcohol

Reactions under the typical mild reaction conditions (room temperature, 1 bar CO) using substrates which contain allyl groups, such as allyl alcohol, allyl ether, allyl acetate or crotyl alcohol, were carried out. In these cases the results obtained were disappointing since no reaction took place. The known ability of

allyl substrates to stabilise palladium species through chelation could, in principle, explain the interference with the desired methoxycarbonylation. Formation of the highly stable 5 membered ring shown in *Figure 2- 14* would stop the reaction.

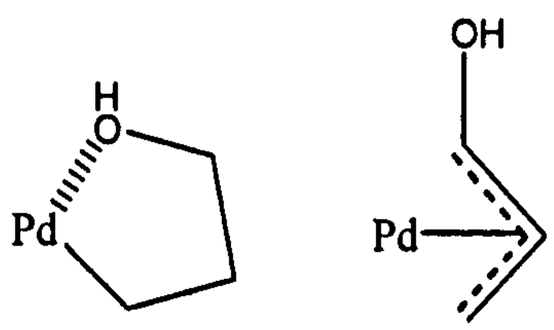


Figure 2- 14: Possible intermediates formed by Pd and allyl alcohol

2.2.2.5. Dienes.

As described in the previous sections, methoxycarbonylation of alkenes using Pd/DTBPMB/H^+ is very effective. The next step was the attempted carbonylation of dienes. Among them, we have mainly looked at butadiene, but also isoprene, 1,6-heptadiene and 2-methyl-1,5-hexadiene have been studied.

Methoxycarbonylation of 1,6-hexadiene produced the monoester in 14 % yield after 14 hours at 40°C and 20 bar of CO. The dicarbonylated product was not detected by GCMS. Neither isoprene nor 2-methyl-1,5-hexadiene reacted under these conditions.

Significant work is being carried out to develop new routes to nylon starting from butadiene. Nylon-6 and nylon -6,6 are formed from the monomers: ε-caprolactam[27] and adipic acid/ hexamethylene-1, 6-diamine[28], respectively. There are potential routes to ε-caprolactam and adipic acid using butadiene.

Dimethyl adipate and methyl-pentenoates are the linear products which can be obtained from methoxycarbonylation of butadiene (*Figure 2- 15*):

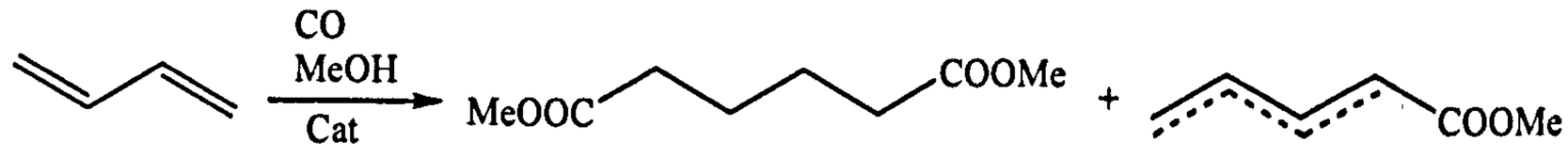


Figure 2- 15: Methoxycarbonylation of 1,3-butadiene

All of the reactions carried out with this substrate by analysis seemed to have gone to completion. However, when the autoclave was opened, butadiene could be smelt as it evaporated, suggesting that the reaction had not gone to completion. This reaction was first attempted using 1,3-butadiene supplied by Aldrich. The results obtained are shown in the Table 2- 13 and Table 2- 14; nevertheless, keeping in mind that the reaction was not complete, these data are only indicative and show the proportion in which each product is formed.

Besides the two expected carbonylation products, 1, 3-butadiene underwent [4+2] Diels Alder reaction to form 4-vinylcyclohexene, which undergoes further isomerisation to 3-ethylidenecyclohexene and 4-ethylidenecyclohexene (*Figure 2-16*).

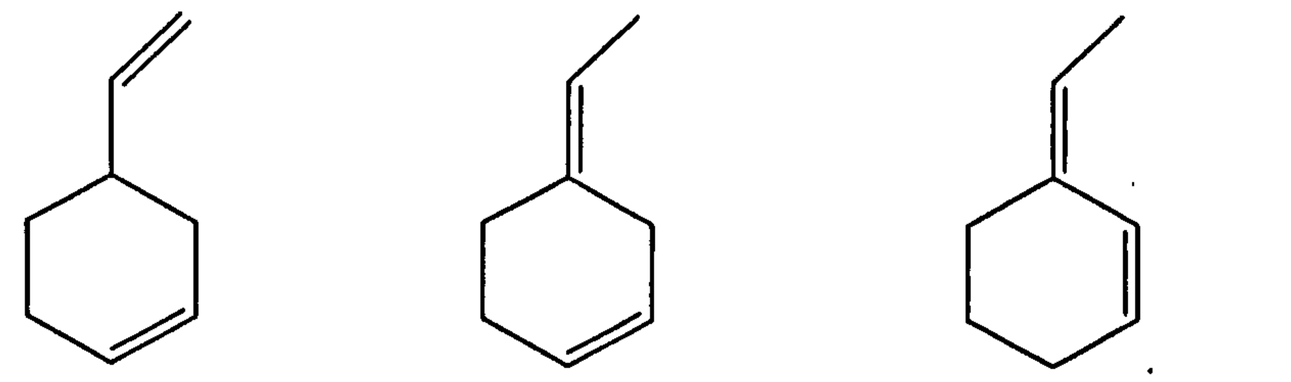
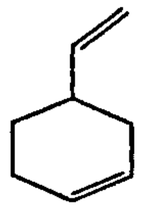
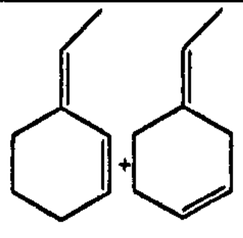


Figure 2- 16: Diels Alder products of butadiene

The data shown reveal that these products are formed selectively at low pressure of CO, suggesting that their formation should not require the presence of CO. However, if CO was absent, a polymer, which seemed to be polybutadiene by solid state ^{13}C NMR, was produced.

By increasing the pressure of CO, the Diels Alder reaction became slower compared to the carbonylation reaction, since the former products turned into minor products favouring the formation of 3-methylpentanote and dimethyl adipate. Unfortunately, reaction conditions suitable for the selective formation of 3-methylpentenoate were not found, since an increase in the pressure of CO inhibits the Diels Alder reaction but also promotes the selective formation of dimethyl adipate. Surprisingly, a small change of 5 bar from 60 to 65 provided a great improvement on the selectivity forming exclusively dimethyl adipate.

Table 2- 13: Methoxycarbonylation of 1, 3-butadiene (Aldrich).

T (°C)	P_{CO} (bar)	T (h)		3-methyl pentenoate	2-methyl pentenoate		9-methoxy-nonenoate	Dimethyl adipate
80[a]	4	6	48	52	0	0	0	0
80[a]	10	6	39	61	0	0	0	0
80[a]	30	6	12	59	0	7	16.6	5.4
80[a]	45	6	5.1	55.4	10.6	2.6	11.1	15.2
80[a]	55	6	13.8	65.1	3.5	1.1	4.7	12
80[a]	60	6	4.6	44.4	10.4	2.6	0	38
80[a]	65	6	0	0	0	0	0	100
50[b]	4	24	92.8	7.2	0	0	0	0
50[b]	10	24	3	75	22	0	0	0
50[b]	20	18	0	0	0	0	0	100
50[b]	40	24	0	0	0	0	0	100

0.2 mmol Pd (0.1 mmol $Pd_2(dba)_3$), 1 mmol DTBPMB, 1.5 mmol MSA, 10 ml MeOH,
(a) 0.042 mol butadiene, (b) 0.02 mol butadiene.

To have a better understanding of this reaction a deeper study was carried out using 1,3-butadiene supplied by BOC gases. Temperature, pressure and catalyst concentration were varied throughout. The substrate was added either as a gas or

as a liquid. Yields to dimethyl adipate and 3-methylpentenoate are shown in Table 2-14.

Once the yields were calculated accurately, they turned out to be extremely disappointing, since the desired products were obtained in <2 % yield. Surprisingly, dimethyl adipate was not detected in many cases, whereas when the substrate was provided by Aldrich, it was the major product. The addition of the substrate as a gas or as a liquid did not lead to an improvement in either the conversion or the selectivity.

Table 2- 14: Methoxycarbonylation of 1, 3-butadiene (BOC gases).

P_{CO} (bar)	T (°C)	Butadiene (mol)	[MeP]x10^3 (M)	Yield MeP (%)	[MA]x10^3(M)	Yield MA (%)
20 [3]	80	0.019(g)	17.6	1.0	0	0
30[3]	80	0.019 (g)	27.6	1.53	0	0
40[1]	80	0.02 (g)	0	0	36.8	1.84
40[3,*]	80	0.02 (g)	84.3	4.68	0	0
50[1]	80	0.019 (g)	48.9	2.72	1.5	0.08
60[1]	80	0.0012 (l)	8.8	7.30	0	0
20[1]	100	0.058 (l)	10.0	0.25	0	0
40	100	0.02 (l)	22.8	1.14	0	0
50	100	0.02 (l)	2.8	0.14	0	0
40	100	0.058 (l)	142.4	3.62	0	0
60	100	0.02 (l)	14.4	0.72	0	0
40[2]	100	0.02 (l)	30.4	1.52	0	0
40	120	0.02 (l)	3.3	0.17	0	0
50	120	0.02 (l)	48.6	2.43	0.01	0.54

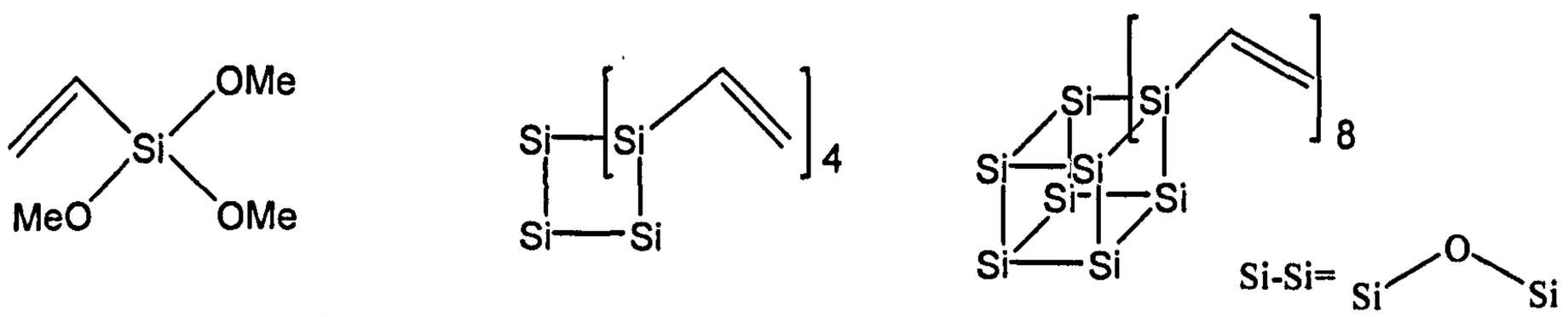
(1): 0.1 mmol Pd, 0.5 mmol L, 1 mmol MSA, 6 h. (2): 0.15 mmol Pd, 0.75 mmol L, 1.5 mmol MSA, 6 h. (3): 0.2 mmol Pd, 1 mmol L, 1.5 mmol MSA, 3 h. (*): 6 h

2.2.2.6. Octavinylsilsesquioxane molecules (POSS).

This work has been carried out in collaboration with Ewan Drylie and Prof. Russell Morris from St. Andrews University.

These substrates are based in vinyl groups bonded to silicon atoms. Therefore, the reactivity of the double bond may be different from those observed for alkenes. However, the attempted carbonylation of these vinyl groups was carried out using the standard catalytic system under different conditions of pressure and temperature.

Three different POSS molecules were used: trimethoxyvinylsilane, tetramethyltetravinylcyclosiloxane and octavinylsilsesquioxane (*Figure 2-17*). The results obtained for each of them are shown in Table 2- 15 and Table 2- 16.



trimethoxyvinylsilane tetravinyltetravinylcyclosiloxane octavinylsilsesquioxane

Figure 2-17: POSS structures.

The presence of three methoxy groups in the first molecule studied will make the double bond more electron rich, in addition to increasing the steric bulk around the coordination site. These factors could hinder bonding to the metal centre. However, once the palladium-alkyl intermediate is formed, the linear palladium-acyl will be very much favoured with respect to the branched due to the steric effects.

We found that under mild reaction conditions the reaction proceeded slower than for simple terminal alkenes (78 % conversion), producing only the desired terminal product. An increase of the bulk around the double bond was introduced by using tetramethyltetravinylcyclosiloxane as the substrate.

Table 2- 15: Methoxycarbonylation of different POSS molecules.

Substrate	T (°C)	P (bar)	t (h)	Conv (%)	Selec (%)
Trimethoxyvinylsilane	25	1	3.25	78	100
tetramethyltetravinylcyclosiloxane	25	1	3	79	100
tetramethyltetravinylcyclosiloxane	25	1	4.5	96	100
tetramethyltetravinylcyclosiloxane	40	1	3	100	100
tetramethyltetravinylcyclosiloxane	80	30	17	100	100

Under 1 bar of CO and at 25 °C, carbonylation of the four vinyl groups was achieved, although the reaction did not go to completion. Due to the difficulty in separating the starting material, the final product and the catalyst, the reaction was carried out under more severe conditions, so that the starting material would react completely. Under 30 bar of CO pressure and at 80 °C the target product was obtained in 100 % yield after 17 hours. However, we found out later that 40 °C and 1 bar of CO were enough to get the same result. Methoxycarbonylation of octavinylsilsesquioxane was carried out in a mixture 1:2, 1:4 or 1:15 MeOH: toluene, due to the low solubility shown by the starting material in MeOH. Given the bulk of the POSS molecule, the steric congestion around the metal would be large and consequently methoxycarbonylation would be slow. Under the usual mild reaction conditions complete conversion was achieved after 6 hours, but unfortunately when scaling up the reaction, poor yields were obtained. Therefore, more severe conditions, 80 °C and 30 bar CO, had to be used. Under these conditions, complete conversion was observed and only the desired product, which has eight acetate groups, was produced.

Table 2- 16: Methoxycarbonylation octavinylsilsesquioxane.

MeOH (ml)	Tol (ml)	POSS (mg)	T (°C)	P (bar)	t (h)	Conv (%)	Selec (%)
5	10	150	25	1	4	37	100
5	10	150	25	1	5.75	69	100
5	10	150	25	1	6	100	100
5	10	100	80	30	17	100	100
5	20	250	80	30	16	100	100
5	20	250	80	30	16	100	100
2	30	400	80	30	16	80	100

2.2.3. DTBPMB catalysis performed under constant pressure

A limitation of the standard autoclaves used for routine catalyst testing is that the stirring employed is via a magnetic bead, which leads to the possibility of poor mass transport. If the reaction is fast and there is insufficient CO being dissolved into the reaction solution the results obtained can be misleading as side reactions may become more competitive. In addition, the sealed autoclave containing all the reactants is heated from room temperature to the reactor temperature so that the reaction conditions are not constant, at least during the early stages. The catalysis was performed in a reactor which has mechanical stirring capable of 1000 rpm. Also it is possible to measure the gas uptake at constant pressure during the reaction and determine the reaction order in substrate. Finally, it is possible to inject the substrate once the reactor is at the required temperature and pressure. The results obtained when the experiments were carried out in a constant pressure autoclave are summarised in Table 2-17. Comparing the first six experiments, in which the only difference is the MSA: Pd ratio, it is observed that although selectivity to the linear ester is similar in all cases (~92%), the

highest conversion was obtained when MSA: Pd = 6.3:1. Under these conditions, the reaction was clearly first order in [1-octene].

When the reaction was carried out under conditions that Drent has patented (experiments 12, 13, 15) the highest conversion observed was 95.7% and selectivities were ~95%. However, if the reaction was run without anisole and at 40 °C and 10 bar CO (experiment 16), it was found that conversion was slightly higher than 96% and selectivity was 95.9%. Under these conditions the l: b ratio was also higher than those obtained under conditions suggested by Drent.[22]

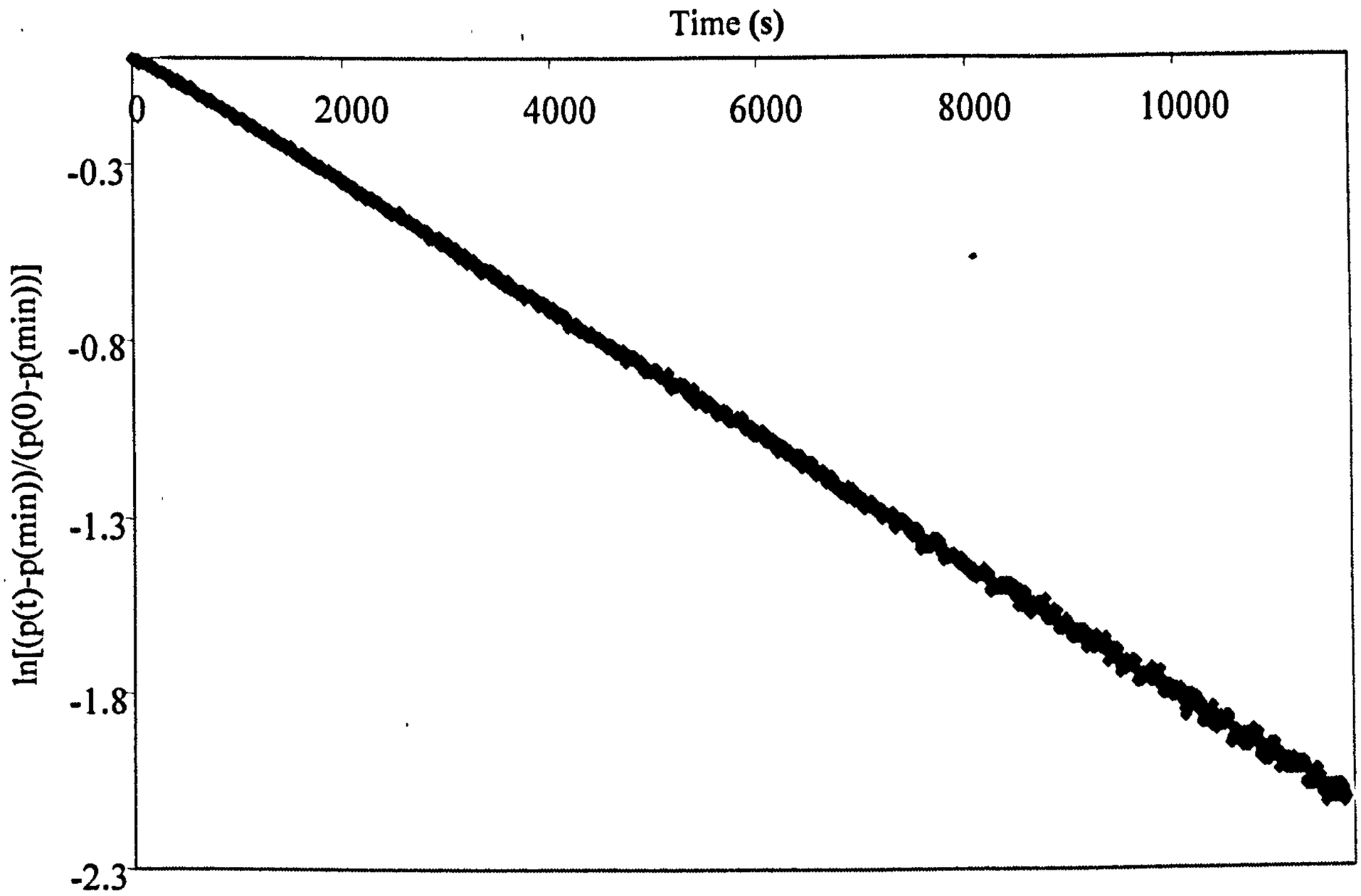
In addition to this, the kinetic plots are different depending upon the reaction conditions. When the reaction is carried out at 30 bar and 80°C, the plot of log [pressure drop in ballast vessel] vs. time is a straight line (see graph 2-1), which means that it is a first order reaction. This line has an excellent fit with a straight line whose slope is –0.0107 giving a first order rate constant of 1.8×10^{-4} s^{-1}. The scale of the plot ends when the reaction is 75% complete and it can be observed that even in the line straight part of the graph, so the reaction is first order at least until 75% reactant, which is very unusual. However, when the reaction was run under milder conditions (10 bar, 40°C), two intersecting straight lines were observed (see graph 2-2). When the reaction has just started, there is only pure 1-octene and its isomerisation is comparable in rate to its carbonylation, that is why the rate constant of CO uptake (corresponding to the direct carbonylation of the terminal alkene) is high ($k = 3.9 \cdot 10^{-4}$ s^{-1}). As the reaction proceeds isomerisation removes much of the 1-octene and all the octenes are in equilibrium. Since carbonylation only occurs when the alkyl intermediate is terminal, 2-, 3- and 4-octene must isomerise back to 1-octene to be carbonylated and therefore the rate

constant for CO uptake is lower ($k=1.7\cdot10^{-4}$ s^{-1}). Both of these observations suggest that carbonylation is fast compared with isomerisation to 1-octene.

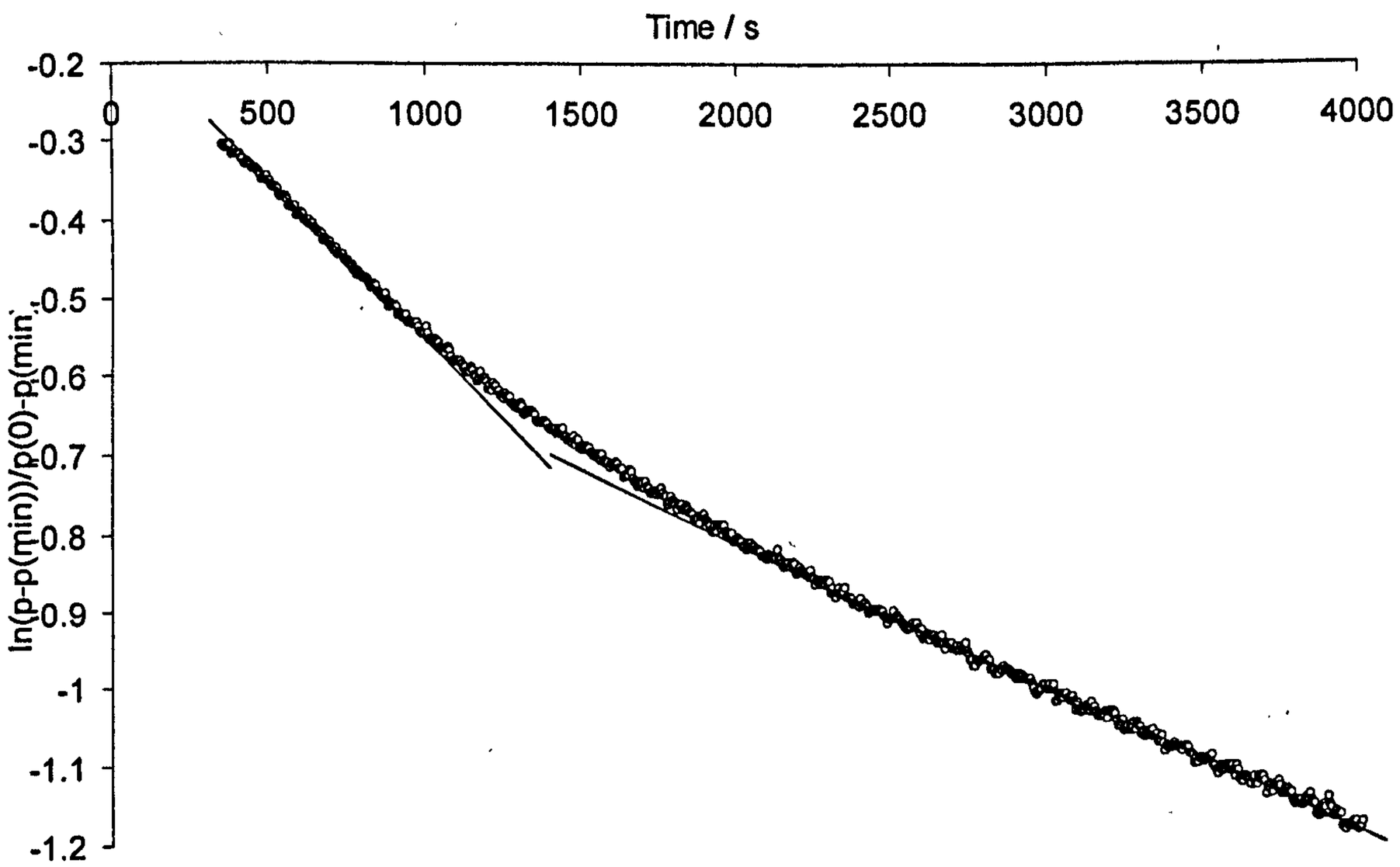
Table 2- 17: Constant pressure autoclave experiments

Expt	MSA:Pd	Solvent[a]	T /°C	P /Bar	T /h	enes /%	2Pr /%	2Et /%	2Me /%	MeNo /%	Other /%	Conv. /%	Selv. /%	L:b	K x 10^4 /s^{-1}	TOF (I) /h^{-1}	Observations on final soln.
6	2.3	MeOH	100	30	6.0	5.9	0.6	0.9	4.0	87.5	1.2	94.1	92.9	13.0 (21.7)	1.6	184	Clear bright yellow soln.
11	2.3	MeOH	100	30	6.5	1.9	0.6	0.9	4.1	91.0	1.6	98.2	92.7	12.8 (22.5)	2.9	333	Clear bright yellow soln.
9	6.3	MeOH	100	30	3.0	1.3	0.6	1.0	4.3	91.2	1.6	98.7	92.4	12.1 (21.2)	8.0	917	Bright yellow soln. + black ppt.
10	6.3	MeOH	100	30	3.0	1.7	0.6	1.0	4.4	90.8	1.6	98.3	92.4	12.1 (20.5)	6.2	711	Bright yellow soln. + black ppt.
7	10.0	MeOH	100	30	6.5	4.2	0.6	0.9	4.1	89.1	1.1	95.8	93.0	13.3 (21.6)	1.8	206	Yellow soln + black ppt.
8	10.0	MeOH	100	30	7.0	2.3	0.6	0.9	4.2	90.8	1.2	97.7	92.9	13.0 (21.4)	2.1	241	Pale yellow soln. + black ppt.
14	2.3	MeOH + A	100	30	0.5	-	-	-	-	-	-	-	-	-	-	-	Clear bright yellow soln.
12	6.3	MeOH + A	100	30	5.0	20.2	0.3	0.5	2.2	75.8	0.9	79.8	95.0	19.2 (34.6)	B	b	Clear bright orange soln.
13	6.3	MeOH + A	100	30	5.0	4.3	0.4	0.7	2.7	90.6	1.3	95.7	94.7	17.8 (33.6)	B	b	Bright orange soln. + orange ppt.
15	6.3	MeOH + A	100	30	6.5	11.0	0.3	0.5	2.2	84.9	1.1	89.0	95.5	21.0 (39.1)	B	b	Clear bright yellow soln.
16	6.3	MeOH	40	10	10.0	3.9	0.3	0.5	1.8	92.1	1.4	96.1	95.9	23.1 (50.6)	3.9 + 1.7	447	Yellow soln + grey solid.

a (MeOH + A) means that methanol (2 mL) + anisole (4 mL) was used as the reaction solvent in place of only methanol (6 mL) i.e. total volume reaction mixture remained constant. b Not simple first order kinetics since both [octene] and [MeOH] are variables. However, the initial rates of reactions employing on MeOH or MeOH/anisole appeared very similar.



Graph 2- 1: Gas uptake plot for methoxycarbonylation of 1-octene at 30 bar and 80 °C.



Graph 2- 2: Gas uptake plot for methoxycarbonylation of 1-octene at 10 bar and 40 °C.

2.2.4. Other structurally related ligands.

Based on the results obtained in the methoxycarbonylation of 1-octene catalysed by Pd-DTBPMB, the effectiveness of ligands structurally related to DTBPMB was examined. An analogous study was carried out using bis(diisobutylphosphinomethyl)benzene (DIBPMB), bis(dicyclopentylphosphino methyl)benzene (DCypPMB) and 1,2-bis(diphenylphosphinomethyl)benzene (DPhPMB) as ligands (*Figure 2- 18*). The length of the backbone and the bite angle remain the same, although the steric constraint decreases, as does the electron donating ability.

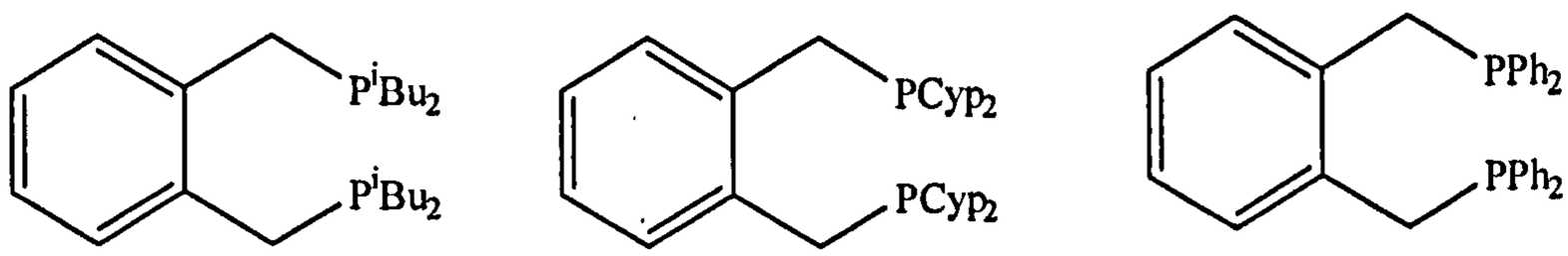


Figure 2- 18: Structure of DIBPMB, DCyPMB and DPhPMB.

By changing the substituents on the phosphorus for less electron donating alkyl groups, like isobutyl or cyclopentyl groups, or for slightly electron withdrawing groups, like phenyl groups, the palladium complex formed would be less electron rich. Thus, the reactivity is expected to change. Secondary alkyl groups are less bulky and provide less steric hindrance than tertiary carbon atoms. Phenyl groups are considered to have a tertiary carbon atom bounded to the phosphorus but as they are flat, the steric bulk is not as effective as that created by a triply substituted carbon atom. Tolman defined the cone angle to evaluate the steric bulk of monophosphines. According to this concept the steric bulk of the monophosphines analogous to those considered for this study is: $^{i}Bu_3P<Ph_3P<^{i}Pr_3P<Cy_3P<^{t}Bu_3P$.[23] Thus, bearing in mind that the cone angle is defined for monophosphines, a correlation between these monophosphines and

the diphosphines could be carried out. Hence, the steric bulk of these bidentate phosphines would be: DIBPMB<DPhPMB<DCyPMB<DTBPMB. In terms of their electron donating properties, the order would be: DPhPMB<DIBPMB<DCypPMB<DTBPMB. As electronic and steric properties of the ligand influence in the catalytic cycle, the results obtained at the end of the reaction may not be the same as for DTBPMB.

A detailed study changing Pd: L ratio, [MSA], pressure, temperature, etc was carried out. The results obtained were surprising and disappointing, since no reaction took place for any of the ligands. This could be rationalised considering either electronic or steric effects. On the one hand less electron donating groups on the phosphorus provide less electron density on this atom, making the metal centre less electron rich. Therefore, the formation of the active hydrido species is disfavoured and the coordination of the alkene more difficult. On the other hand, neither the bite angle nor the flexibility of the backbone seems to be determinant for the carbonylation reaction, but steric congestion around the palladium coordination sphere appears to be essential for activity as reported by Whiston.[19]

2.2.5. Hydroxycarbonylation of 1-octene.

The highly selective hydroxycarbonylation of alkenes to carboxylic acids for use in detergents as ethoxylates or via hydrogenation to alcohols is also an important target. Further hydrolysis of the esters formed by palladium catalysed methoxycarbonylation of alkenes will lead to carboxylic acids. Direct hydrocarbonylation of alkenes to long chain carboxylic acids instead of esters was attempted. For this purpose water had to be used as a nucleophile. Unfortunately, the catalyst is not soluble in water. This problem was overcome

by using acetone was as the solvent and water as a reactant. However, due to miscibility problems only a small amount of water can be mixed with acetone to give a one phase solution. The results obtained are shown in Table 2- 18. The reaction time was always 20 hours for two reasons: (1) water is less nucleophilic than any alcohol, therefore, less reactive for this reaction and (2) not being able to be used as solvent, the concentration of water was low, although enough to complete the reaction. The formation of 1-methylethylenylnonanoate (*Figure 2-19*) arose from the nucleophilic attack of the enolic form of the acetone, since a tautomeric equilibrium exists between both the keto and the enol form. Even after 20 hours the reaction was not complete, although very good selectivity was observed in all cases. Under low pressure (10 bar) and independently of the temperature, conversion was >80 % and the desired linear acid was produced in >95 % selectivity. However, an increase of pressure exerted an inhibiting effect, reducing the conversion dramatically but not affecting the selectivity. More importantly, the catalyst was stable under reaction conditions.

Table 2- 18: Hydroxycarbonylation of 1-octene.

[Pd] (M)	[L] (M)	[H_2O](M)	Solv	T (°C)	P (bar)	T (h)	Conv (%)	Sel (%)
7.7×10^{-3}	0.04	4.3×10^{-6}	THF	80	20	3	2	100
4.2×10^{-3}	0.02	4.6×10^{-6}	Acetone	70	20	3	46	>99
8.3×10^{-3}	0.04	4.6×10^{-6}	Acetone	50	7	20	88[(1)]	98
4.3×10^{-3}	0.02	2.4×10^{-6}	Acetone	40	10	20	81	98
4.3×10^{-3}	0.02	2.4×10^{-6}	Acetone	40	20	20	45	98
4.3×10^{-3}	0.02	2.4×10^{-6}	Acetone	70	10	20	88	95
4.3×10^{-3}	0.02	2.4×10^{-6}	Acetone	70	20	20	76	96

(1): 1-methylethylenylnonanoate was present at a level of 6%

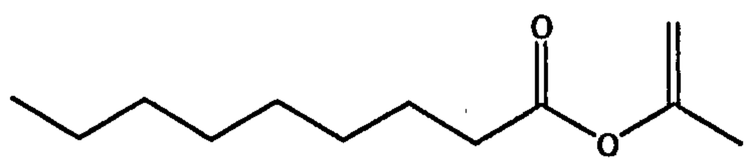


Figure 2- 19: Structure of 1-methylethylenylnonanoate.

2.2.6. Mechanistic studies.

2.2.6.1. Isomerisation in CH_3OD with no CO

The methoxycarbonylation reaction of internal octenes showed extremely high selectivity towards the linear ester. Thus, isomerisation of the internal double bond to the terminal position must occur. Table 2-19 shows that both methyl nonanoate or octenes incorporate deuterium atoms from MeOD. To gain a greater understanding of the formation of isomerised alkenes a reaction in CH_3OD in the absence of CO was carried out to see if the isomerisation products incorporate deuterium. No D incorporation onto any carbon atom of the isomerised alkenes could be detected. To understand these data we propose the mechanism shown in *Figure 2-20.*

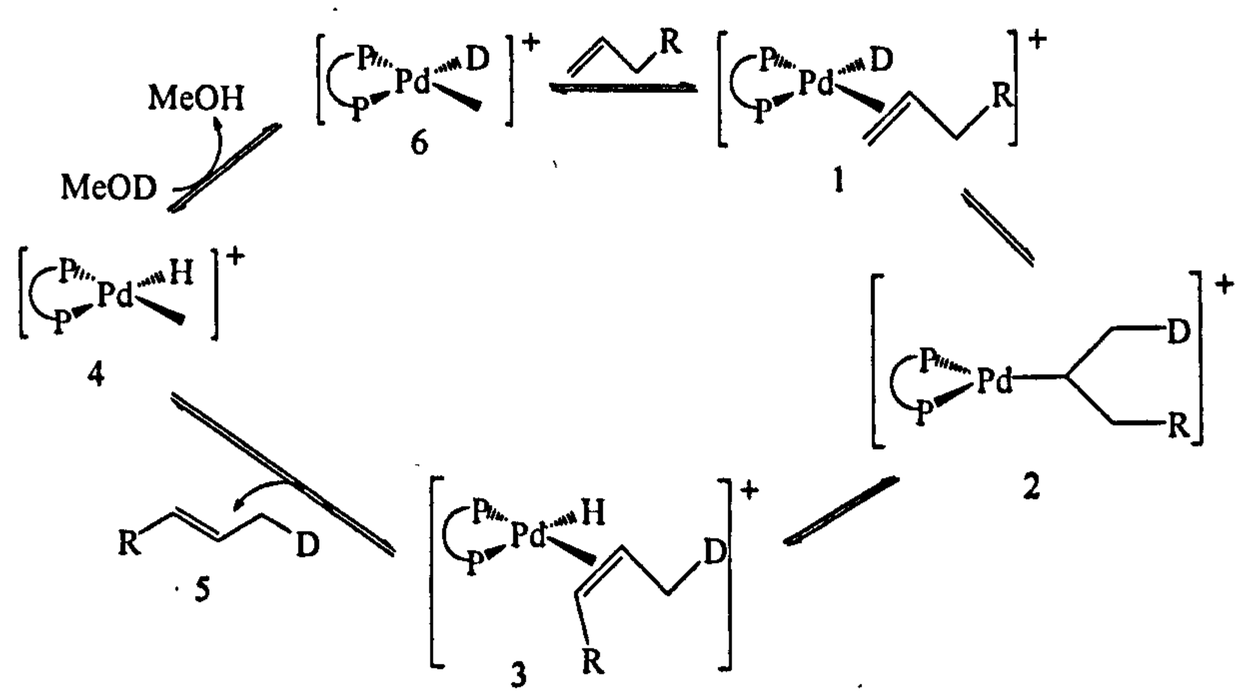


Figure 2-20: Mechanism for isomerisation of alkenes

Coordination of the alkene to the metal centre leads to species 1. Migration of the deuterium atom onto the terminal carbon atom of the alkene leads to species 2. β-hydride elimination from the C_1 takes place as a consequence of the higher rate of this abstraction over the one from C_3 leading to species 3.[26] The deuteriated alkene (5) so formed is released regenerating the hydrido-Pd complex (4), which may coordinate another molecule of alkene (terminal or internal).

The rate of exchange of species 4 with MeOD to form species 6 must be much slower than coordination of alkene to form species 3 since no deuteriated isomerised alkenes were detected. The bulk of the reaction then occurs from the hydride 4 and no further D is incorporated into the isomerised alkenes. Therefore, there will be as many deuteriated alkenes as palladium atoms and this is not enough to be detected by GC.

2.2.6.2. Carbonylation in CH_3OD.

When catalytic reactions are studied it is important to know what the mechanism of the reaction is so that the reaction can be optimised leading to a better understanding of why one product is obtained in higher amounts than others.

For this reason we started to use deuteriated methanol in our experiments. In terms of the products distribution, there is no difference between MeOH and MeOD, i.e., conversion, selectivity and l: b ratio are quite similar but the amount of deuterium in the product can give important mechanistic information.

Using a catalyst prepared *in situ* from $[Pd_2(dba)_3]$, DTBPMB and methanesulfonic acid in MeOD, some experiments were carried out under different conditions. The results of these reactions are summarised in Table 2-19.

Complete conversion of octenes was achieved when the reaction was carried out in MeOD at 80 °C under 30 bar of CO for 3 hours (entry 1). Careful analysis of the products obtained showed the formation of d^0-d^{16}-methyl nonanoate. Nevertheless, the d^1 isomer was produced in a higher proportion than expected according to a statistical distribution. However, if the reaction is carried out under the same conditions but in a mixture 1 to 4 MeOD to toluene, labelled isomerised alkenes are recovered at the end of the reaction and the d^1 isomer is no longer

predominant (entry 2). Similar results were obtained when 2-octene was used as the substrate (entry 3). A reaction carried out under catalytic conditions (room temperature and 1 bar of CO) in MeOD (entry 4), gave the monodeuteriated ester as the major product with smaller amount of d^0, d^2 and d^3.

Table 2- 19: Percentage of d_n products

	Methyl Nonanoate				Trans-2-octene			
	1	2	3	4	1	2	3	4
d_0	2.1	5.4	5.6	25.8	-	2.1	2.5	12.5
d_1	7.7	16.3	16.1	59.7	-	9.6	9.6	26.1
d_2	4.9	20.2	20.1	10.0	-	18.8	17.8	34.1
d_3	4.7	21.4	21.7	4.5	-	24.4	23.4	27.3
d_4	4.6	17.8	17.5		-	21.8	20.3	
d_5	4.9	10.9	11.6		-	13.7	14.2	
d_6	5.7	5.8	5.6		-	6.6	9.6	
d_7	7.0	2.3	1.9		-	2.5	2.5	
d_8	5.2				-	0.5		
d_9	9.7				-			
d_{10}	11.5				-			
d_{11}	11.2				-			
d_{12}	9.5				-			
d_{13}	6.7				-			
d_{14}	3.4				-			
d_{15}	1.1				-			
d_{16}	0.1				-			

1: 80°C, 30 bar, 0.75 h, MeOD; 2: 80°C, 30 bar, 3h, MeOD: toluene (1: 4); 3: 2-octene, 80°C, 30 bar, 3 h, MeOD: toluene (1: 4); 4: RT, 1 bar, 4.25 h

As previously mentioned, at 80 °C and 30 bar of CO multiply deuteriated esters (0-16 D atoms) were produced with d^1 being present in a higher proportion than expected statistically. *Figure 2-21* shows the parent ions from methyl nonanoate formed using CH_3OD. Note the increased peak at *m/z* 173 arising from d^1-methyl nonanoate. This is more obvious from the total ion count, inset. The sharp peak is from d^1-methyl nonanoate, whilst the broad envelope contains the other isomers. Notice that the more highly deuteriated isomers (higher mass) elute from the GC column first. Traditionally, two mechanisms have been considered to be operating

in this reaction: the carbomethoxy mechanism and the hydride mechanism. However, only the latter is able to rationalise the formation of d^0-methyl nonanoate.

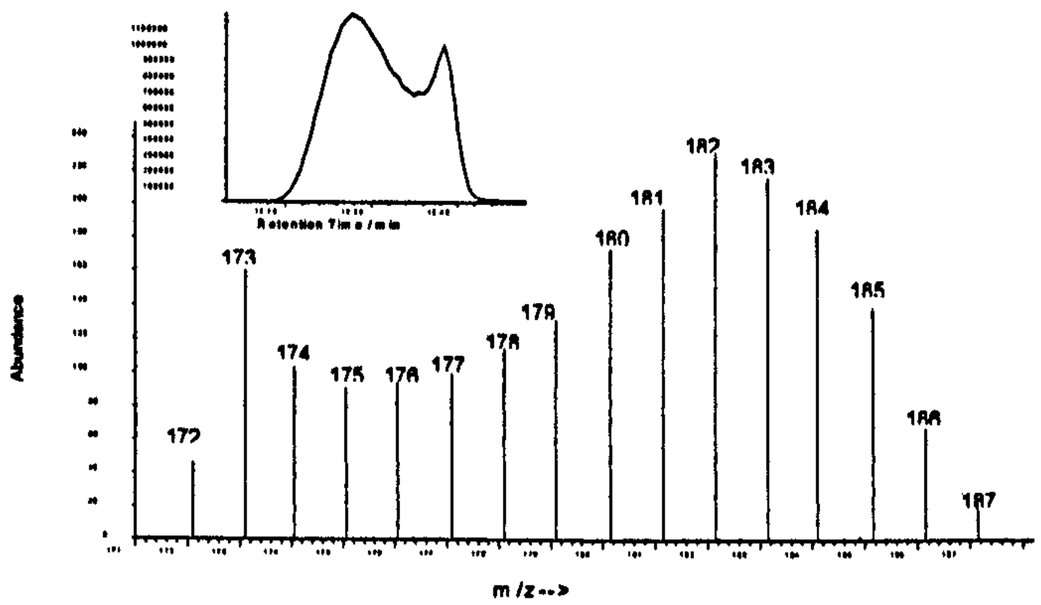


Figure 2-21: Mass spectrum of multiply deuteriated methyl nonanoate

The carbomethoxy mechanism (*Figure 2-22*) starts with a palladium-methoxy species (7). The vacant site is filled by CO to lead to species (8). Migration of methoxide onto the carbonyl (9) and coordination of the alkene and insertion of the alkene into the Pd-COOMe bond forms the intermediate (10). Regeneration of the initial species and release of the ester (11) requires incorporation of the deuterium atom to the palladium-carbon bond in species 10. Thus, there is no possible route that leads to the formation of d^0 methyl nonanoate when the reaction is carried out in MeOD, at least in the early stages of the reaction.

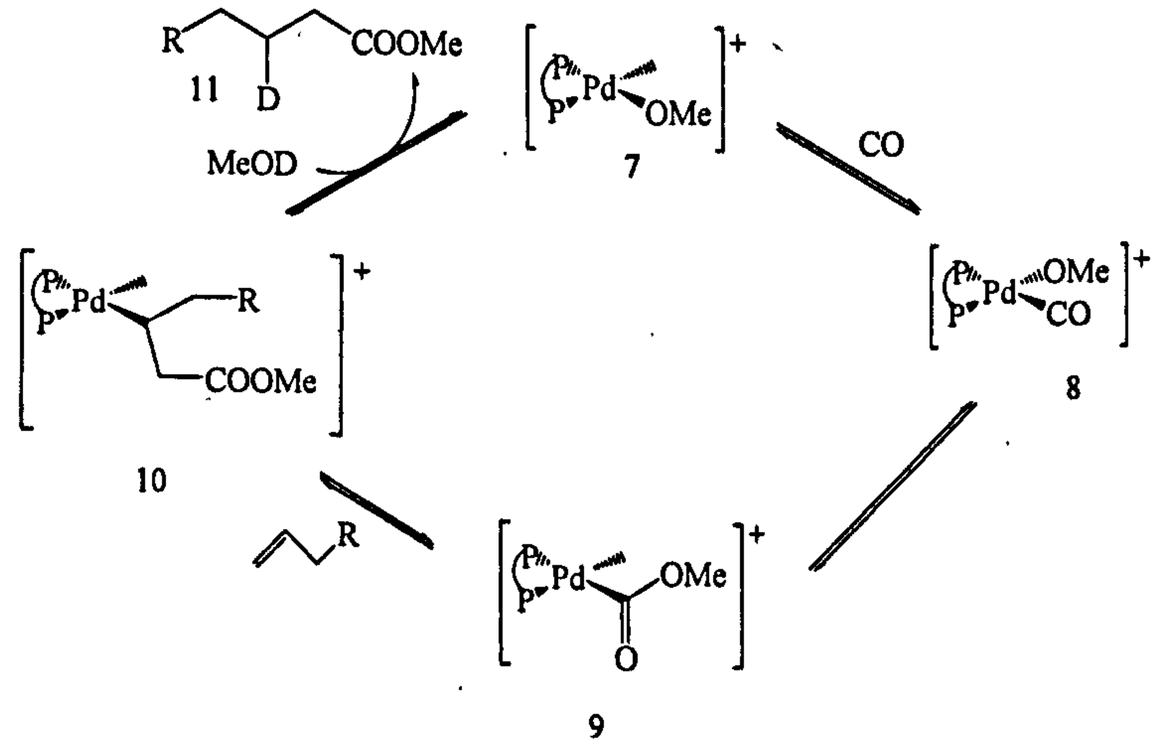


Figure 2-22: Carbomethoxy mechanism.

The hydride mechanism does permit the formation of the d^0 ester at the beginning of the reaction and it can also explain the formation of the monodeuteriated ester in a higher proportion than what expected according to a statistical distribution.

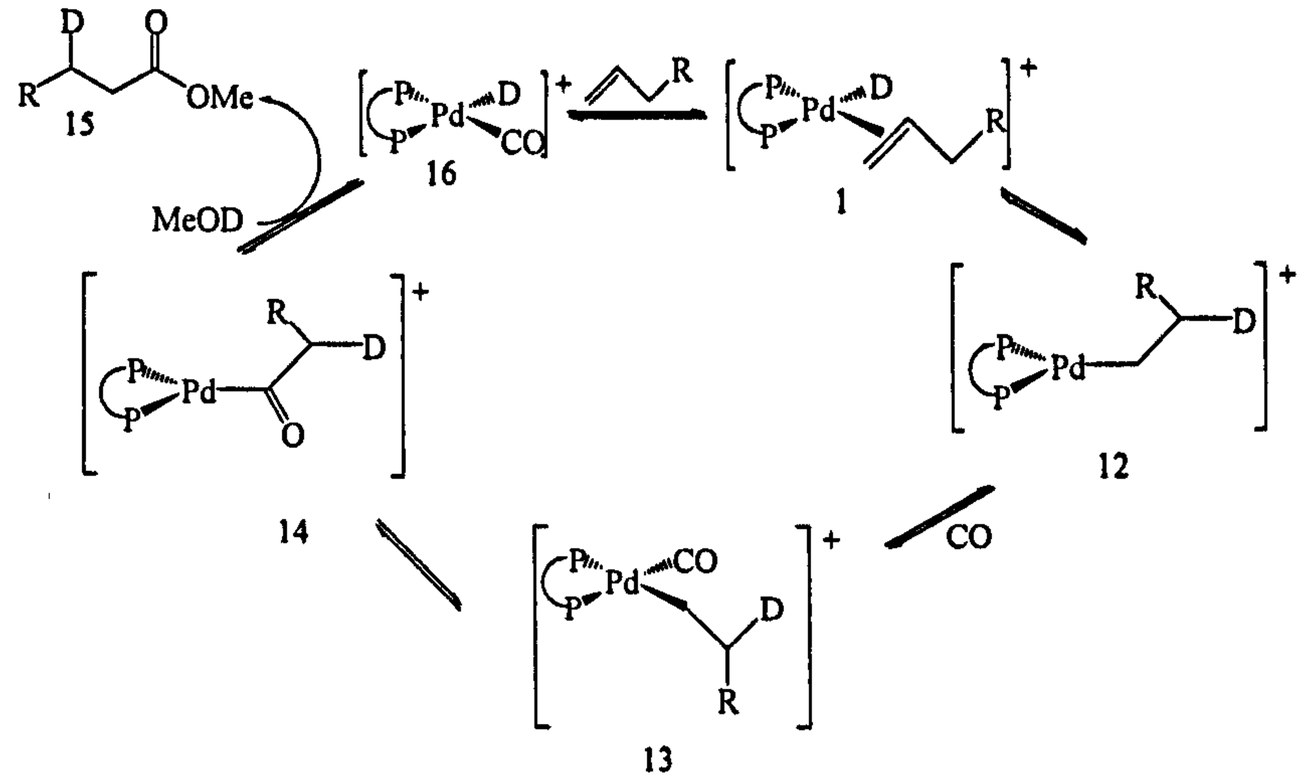


Figure 2-23: "hydride" mechanism: formation of d^1-methyl nonanoate

The hydride cycle (*Figure 2-23*) is initiated by a palladium-deuteride species (16). Replacement of CO by an alkene forms species (1). Migration of the deuterium atom onto the alkene leads to the palladium-alkyl intermediate (12), which in the presence of CO forms species (13). Migratory insertion of CO onto the palladium-carbon bond forms the palladium-acyl intermediate (14). Nucleophilic attack of methanol onto the acyl regenerates the initial species (16) releasing d^1-methyl nonanoate (15). Thus, the production of the monodeuteriated ester is attributed to the direct carbonylation of a terminal alkene probably at the beginning of the reaction. However, species (13) may also undergo β-hydride elimination to form a palladium-hydride intermediate (17), which contains a deuteriated alkene. This deuteriated alkene can be replaced by a non-deuteriated alkene leading to species (18), which will enter the cycle to form d^0-methyl nonanoate (*Figure 2-24*).

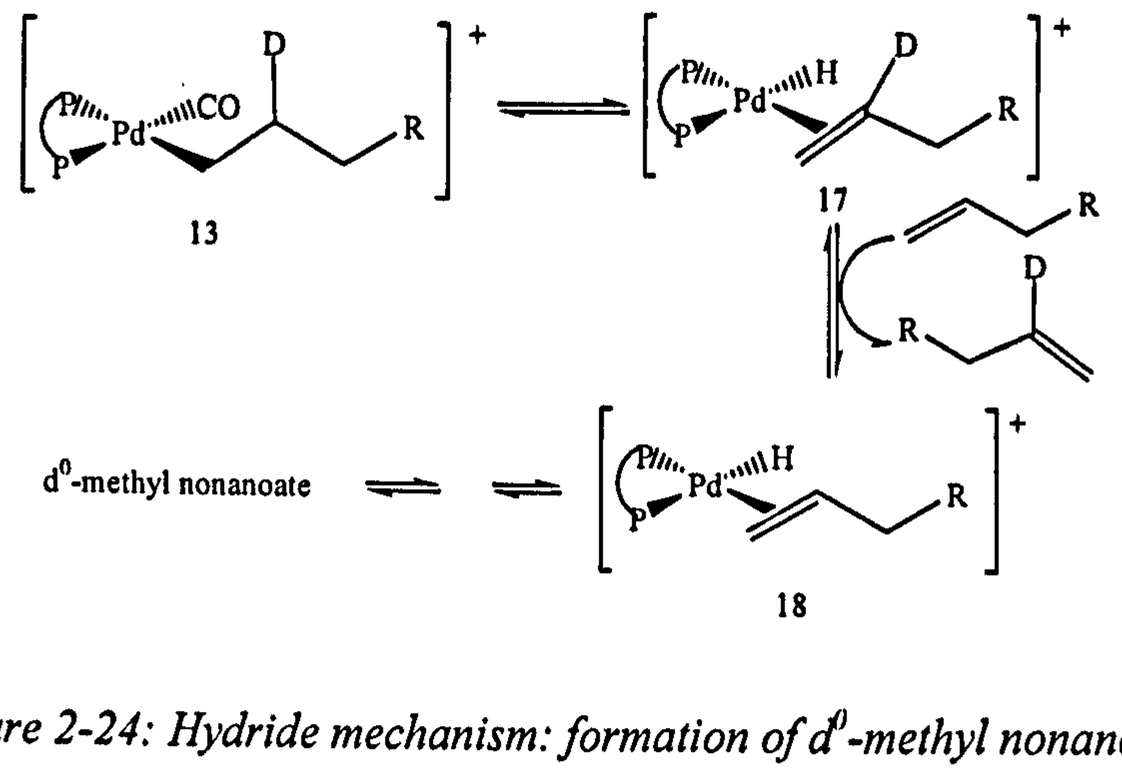


Figure 2-24: Hydride mechanism: formation of d^0-methyl nonanoate

These observations add further support to the suggestion made on the basis of kinetic measurement (see section 2.2.3) that methyl nonanoate forms by two different pathways: directly from 1-octene and by tandem isomerisation-carbonylation of isomerised internal octenes. The multiply deuteriated products on the other hand are formed by isomerisation/ carbonylation of the internal alkenes, which in turn form by metal catalysed isomerisation of the terminal alkene.

We have shown that deuterium incorporation does not occur in the absence of CO. However, Table 2-19 showed that octenes incorporate deuterium onto the chain in the presence of CO. We propose the following mechanism for the formation of monodeuteriated and multiply deuteriated alkenes (*Figure 2-25* and *Figure 2-26*).

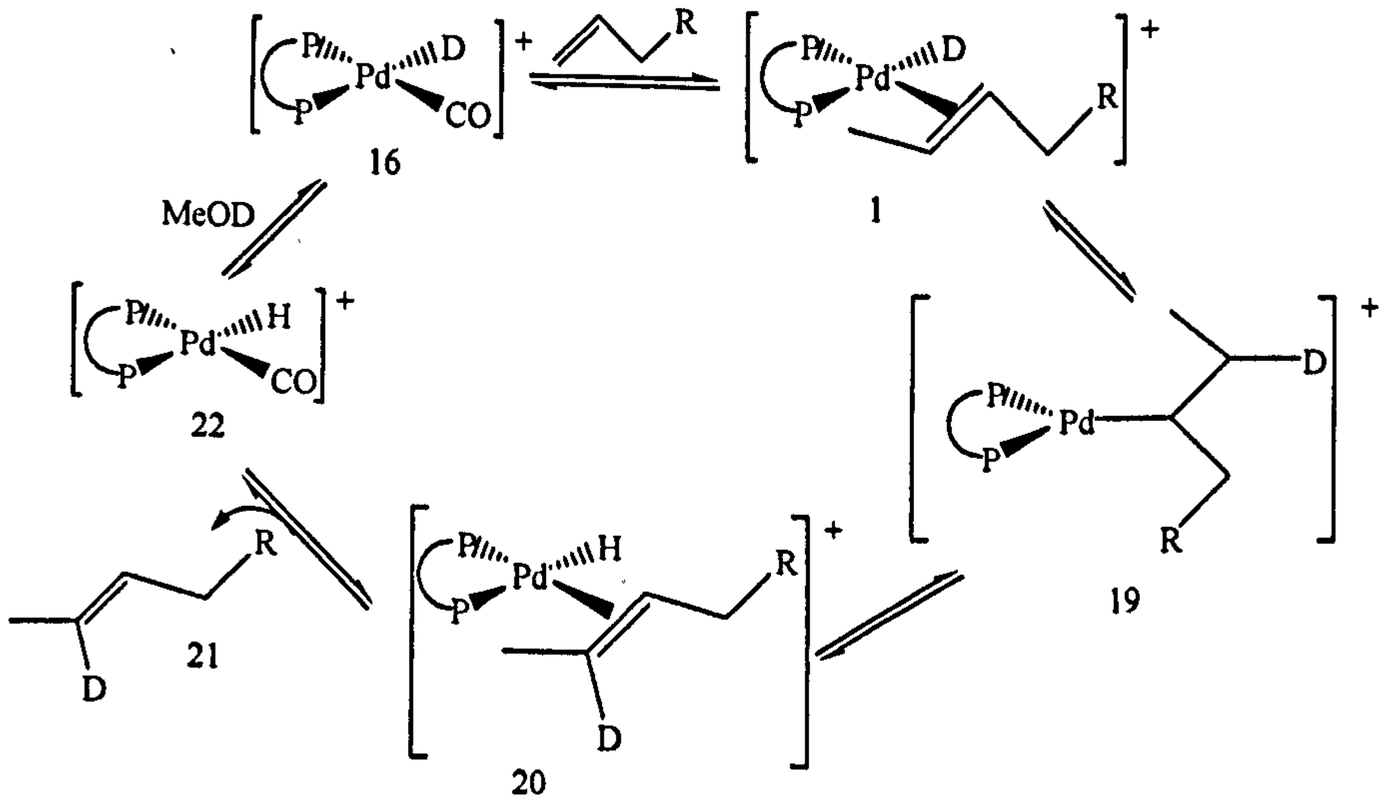


Figure 2-25: Formation of deuteriated internal alkenes.

Replacement of CO by a non labelled alkene in the initial deuteride carbonyl palladium species (16) leads to the formation of species (1). Migration of the deuterium atom onto carbon 2 forms intermediate (19), which may undergo β-hydride abstraction from carbon 2 to form species (20). This leads to the formation of a monodeuteriated internal alkene (21), regenerating the initial hydrido carbonyl palladium species (22).

The H/D exchange when the CO is coordinated (species 22 and 16) must be fast relative to the coordination of internal alkenes with replacement of CO in species 22. Once the H/D exchange has taken place, the CO is replaced by the alkene. Thus, the hydrido species entering the catalytic cycle will always contain Pd-D instead of Pd-H.

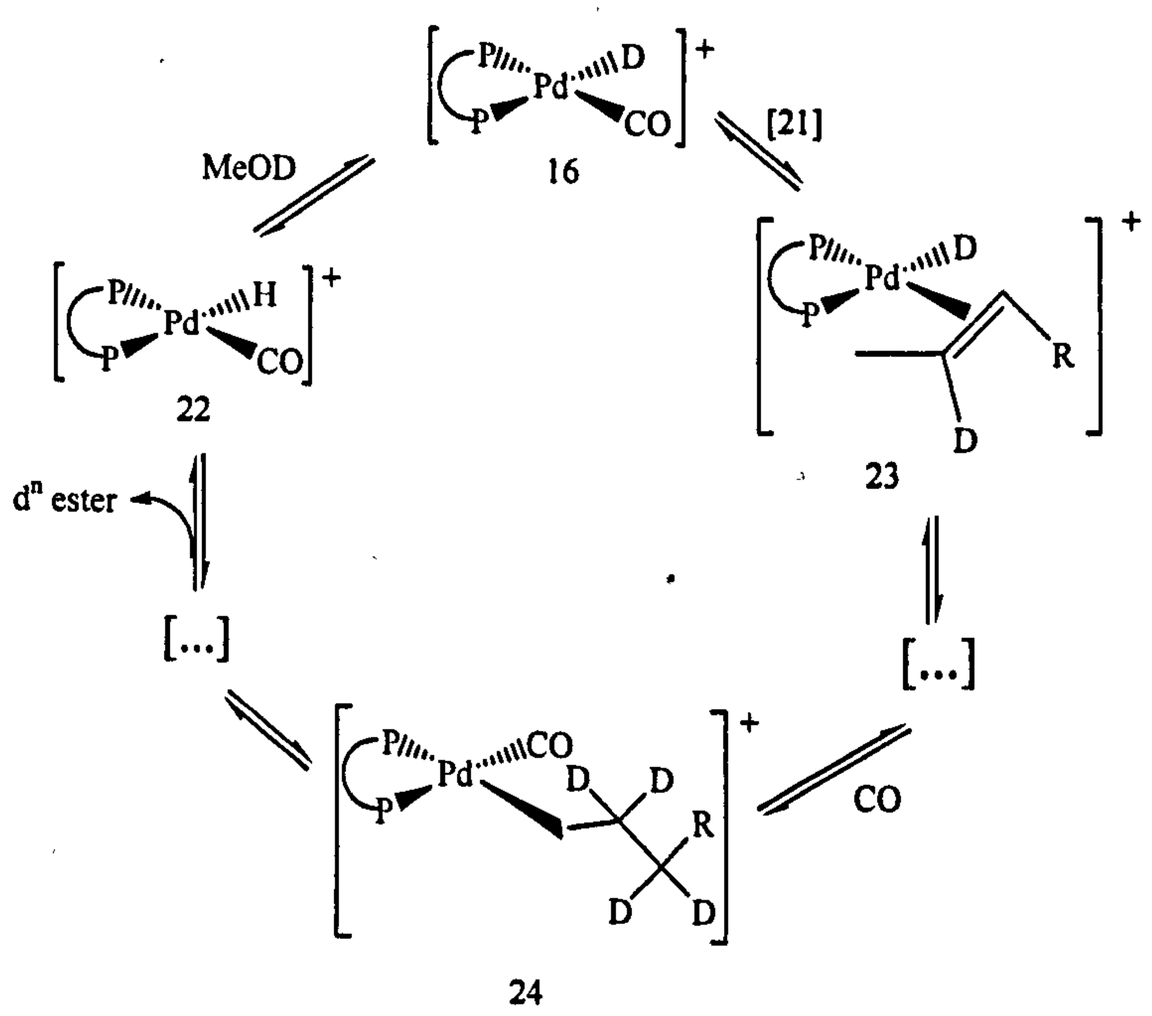


Figure 2-26: Formation of multiple deuteriated esters

If 16 is formed it is possible to obtain isomerisation products containing D. When an isomerised alkene is coordinated to Pd to form species 23, the deuterium is incorporated into an internal position. Multiple deuteriation of the alkenes implies that alkene is displaced from 20 by CO and H/D exchange occurs before

recoordination of the alkene. The amount of isomerisation is reflected in the amount of multiply deuteriated ester product formed. This is quite large under conditions of high pressure and temperature, but much lower at 1 bar and 20°C.

The relative rates of isomerisation and carbonylation of the terminal alkene are determined by the ratio of the rates of conversion of 1→20 and of 1→14. Since the latter involves CO and the former does not, it is expected that more monodeuteriated product should be obtained at higher CO pressure, as is observed.

At higher pressures, the concentration of methanol has a marked effect on the ratio of d^1: multiply deuteriated ester. At low concentration of MeOH, very little excess d^1 ester is formed but at high [MeOH], much more is obtained. This suggests that all the steps prior to attack of methanol are reversible and probably that attack of MeOH is rate determining. The last step in the methoxycarbonylation might be nucleophilic attack of $^-$OMe to the palladium acyl intermediate. This action will be easier if the electron density in the acyl carbon atom is low. To obtain less electron density in the acyl it is necessary to decrease the electron density in the palladium since DTBPMB is a highly electron donating ligand.

2.2.7. High linear selectivity

Considering the possible influence of the electronic effects one of the two metal-alkyl isomers must be electronically more stable than the other one. It must be noted that in one the carbon atom attached to the metal centre is a primary carbon atom, whereas in the other isomer the carbon atom attached to the metal centre is secondary, making this intermediate less stable. In the case of an alkene no

electronic difference between both isomers is observed. Steric effects must account for the different stabilities of the two isomers. Due to the bulkiness of the groups attached to the phosphorus atom and hence the small pocket angle, when the ligand coordinates to the metal centre, it does not leave much space for the other ligands and for the alkene (*Figure 2-30*). The most favoured way of coordination of the alkene is the one which has less steric hindrance, which in this case places the metal in the terminal position leading to the linear alkyl intermediate.

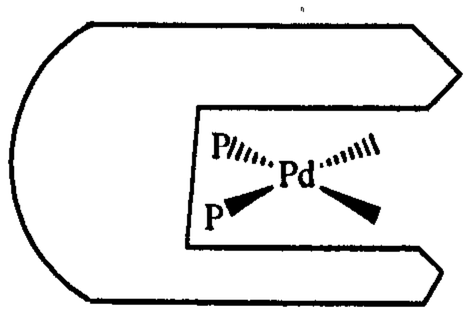
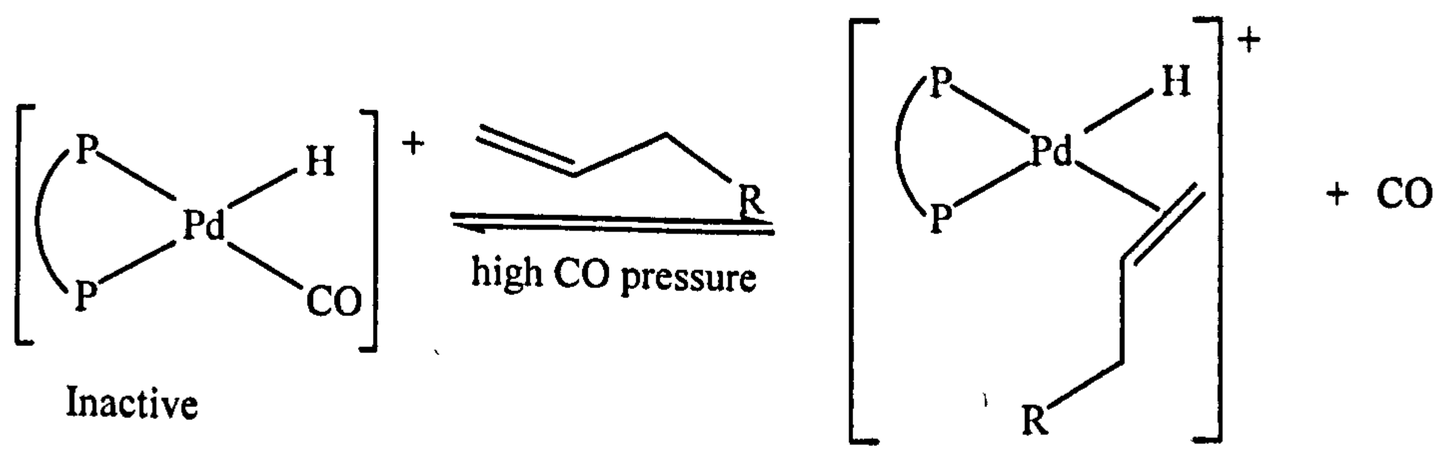


Figure 2-30: Pocket angle of DTBPMB.

In an attempt to rationalise the higher selectivity observed at low pressure we propose that the hydrido-carbonyl species is inactive, whereas the hydrido-alkene species is the active species. Competition between alkene and CO coordination to the $[Pd(DTBPMB)H]^+$ would favour the alkene and hence produce higher rates at low CO pressure (*Figure 2-31*). Therefore, high pressure would favour the formation of the inactive hydrido-carbonyl species.



Inactive

Active

Figure 2-31: Equilibrium set between the hydrido-carbonyl species and the hydrido-alkene species.

2.3.Aminocarbonylation of alkenes

Amides constitute a very key group of compounds owing to their importance as intermediates in the industrial synthesis of a great variety of products, such as detergents and thickeners. Such compounds are usually produced by carbonylation of amines or by carbonylation of alkenes and alkynes with amines. Either homogeneous catalysis or heterogeneous catalysis with several metals can be used for this purpose. Regarding the homogeneous catalysis, there are many reports on the Pd-catalysed aminocarbonylation of arylic, vinylic and allenic substrates[29,30,31]. Platinum is also employed for the hydration of nitriles to amides.[32] Supported Ru catalysts have recently been used for the reaction of CO, ammonia and ethene and cobalt on charcoal has been reported to be very active on the aminocarbonylation of alkenes with aniline.[33] However, the conditions used for these reactions are very harsh (200 °C, 150 bar) and there is interest in moderating them. For this reason we have investigated the possible activity of Pd-DTBPMB complexes on the catalytic synthesis of *N*-phenyl nonanoyl amides from octenes and aniline.

2.3.1. Aminocarbonylation of 1-octene

The aminocarbonylation reaction was carried out in diethyl ether using aniline, 1-octene, carbon monoxide and $PdCl_2$-DTBPMB as the catalytic system. The yield of amide depends upon the concentration of catalyst, concentration of amine, pressure of CO, temperature and reaction time. A detailed study was carried out to establish the optimum conditions.

2.3.1.1. Effect of the Pd:DTBPMB ratio

Carbonylation of 1-octene in the presence of aniline produces methyl *N*-phenyl nonanoyl amide as the linear product and *N*-phenyl-2-methyl octanoyl amide as the branched product, usually the former is the desired product.

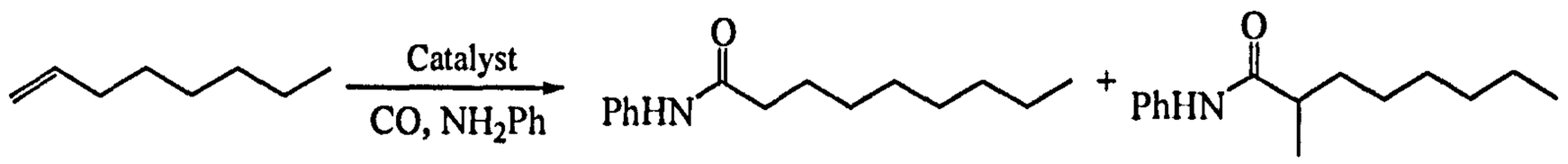


Figure 2-32: Aminocarbonylation of 1-octene.

The ratio Pd: DTBPMB was raised from 1:1.1 to1: 10.5, with the temperature and the pressure held constant at 100 °C and 30 bar of CO respectively. Table 2-20 lists the experimental conditions used and the results obtained.

Table 2- 20: Effect of the Pd:DTBPMB ratio

Pd (mmol)	DTBPMB (mmol)	Aniline (mmol)	1-oct (%)	Isom (%)	l (%)	b (%)
0.2	0.25	22	15	45	40	0
0.2	1.05	22	4	51	45	0
0.2	2.1	22	1	79	20	0

T= 100 °C, P= 30 bar, t= 3 h.

The linear amide was the only product detected. The conversion to amides increased slightly from Pd:DTBPMB=1:1.1 to 1:5 but decreased dramatically at ratio 1:10.1, whereas the isomerisation increased significantly on going from ratio 1:1.1 to 1:10.1 (*Figure 2-33*). Although the most effective performance of the catalyst was provided by a Pd: DTBPMB= 1: 5, a Pd: DTBPMB= 1: 1 was used for the rest of the study. Surprisingly, a large excess of phosphine appeared to have a suppressing effect on the carbonylation and a promoting effect on

isomerisation. It is noteworthy that fast catalyst decomposition occurred to yield metallic palladium even at DTBPMB: Pd= 10:1.

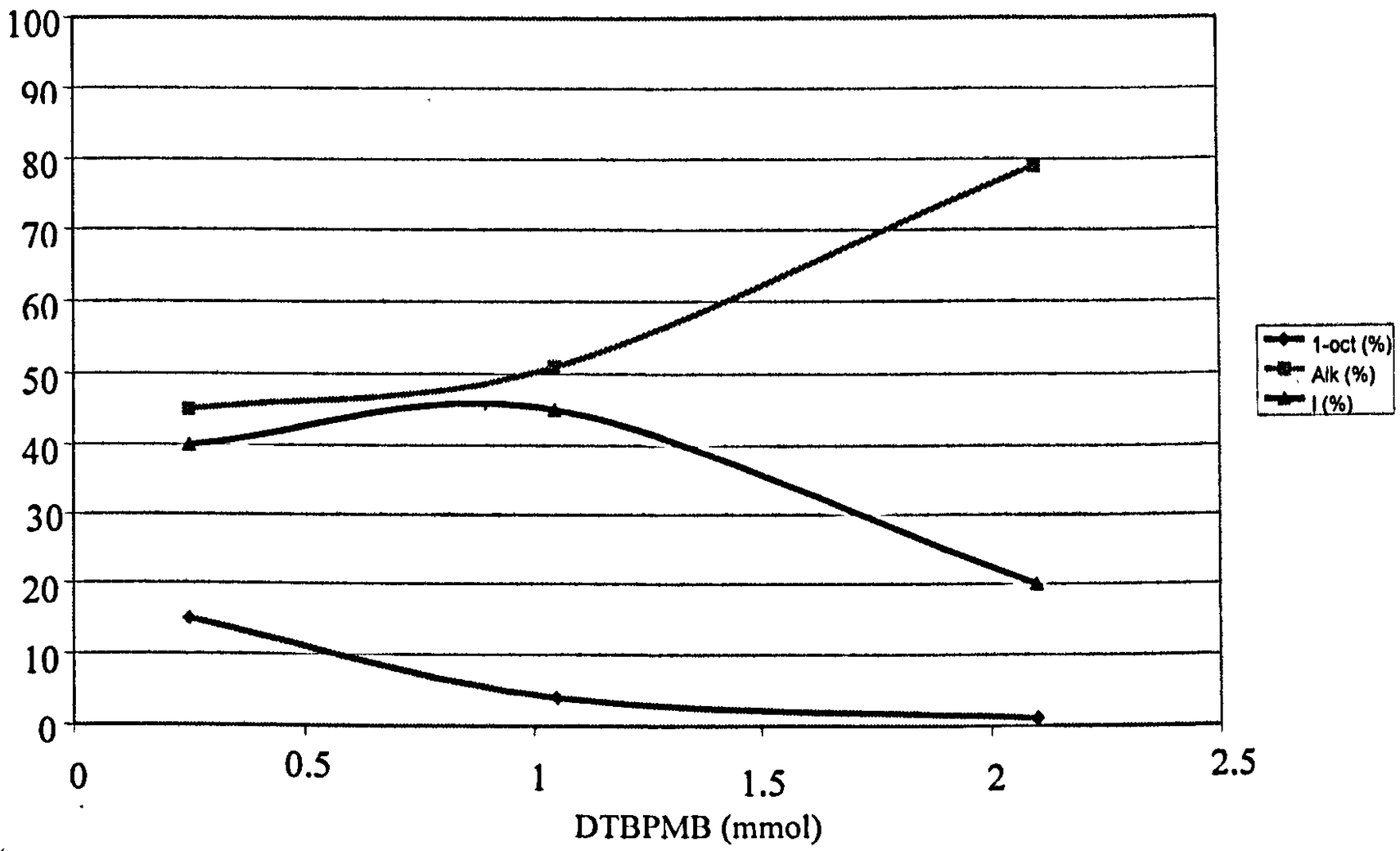


Figure 2-33: Effect of the Pd:DTBPMB on the aminocarbonylation of 1-octene.

2.3.1.2. Effect of the pressure and the temperature

Given the harsh reaction conditions reported in the literature for this reaction, the reaction was carried out under different CO pressures and temperatures to check the effectiveness of this catalytic system.

Maintaining a constant pressure of 30 bar, the temperature was dropped from 100 °C to room temperature, and maintaining the temperature at 100 °C, the pressure was dropped from 30 bar to 2 bar. The results obtained are shown in Table 2- 11 and *Figure 2-34*.

Table 2- 11: Effect of the pressure and temperature

Pd (mmol)	DTBPMB (mmol)	T (°C)	P (bar)	Amine (mmol)	t (h)	1-oct (%)	Isom (%)	l (%)	b (%)
0.2	0.25	100	30	11	3	11	51	38	0
0.2	0.25	rt	30	11	3	100	0	0	0
0.2	0.25	100	10	11	3	0	32	65	3
0.2	0.25	100	2	11	22	100	0	0	0

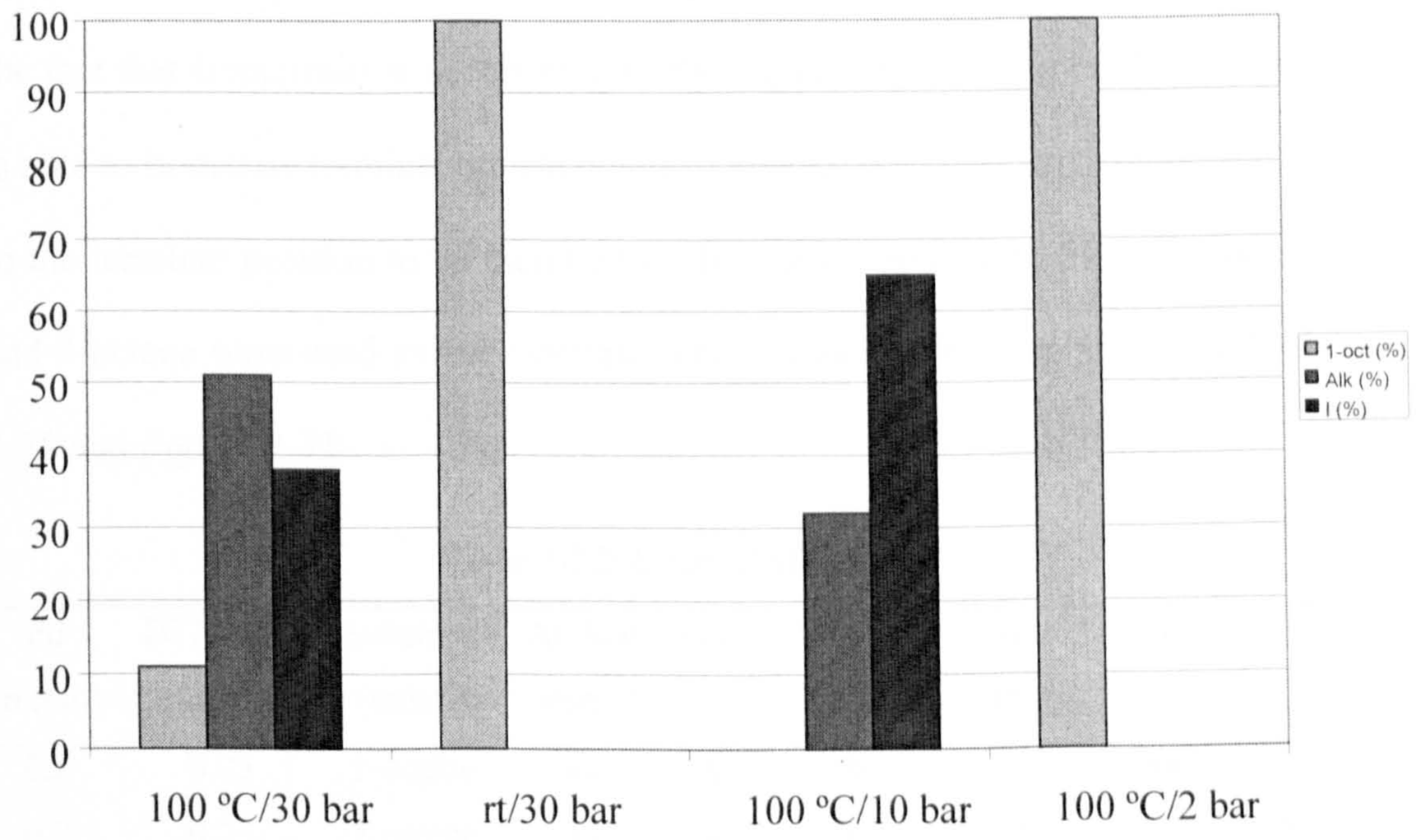


Figure 2-34: Effect of the temperature and the pressure.

Under 30 bar and 100 °C not only did some 1-octene remain unreacted (11 %) but also a large amount of isomerisation products was detected (51 %). The linear amide was formed selectively (38 %). A decrease of the temperature from 100 °C to room temperature resulted in the inhibition of both the isomerisation and the carbonylation reactions. The reduction of the pressure from 30 to 10 bar, resulted in an increase of the activity of the catalyst, since complete conversion, lower

isomerisation (32 %) and a higher selectivity to linear amide (65 %) were achieved. Further reduction of the pressure to 2 bar had a suppressing effect on the reaction, despite the longer reaction time (22 hours), suggesting that a minimum pressure of CO is necessary to initiate the reaction. In all cases catalyst decomposition occurred.

2.3.1.3. Alkenes other than 1-octene

As discussed for methoxycarbonylation, high linear selectivity is achieved despite the fact that isomerisation occurs effectively, suggesting that this catalytic system is able to isomerise terminal double bonds to internal positions and isomerise back to the terminal position to be then trapped by carbon monoxide. Hence, 2-octene and 4-octene were used as the substrate. The results obtained are shown in Table 2-22 and *Figure 2-35*.

Table 2-22: Internal alkenes

Pd (mmol)	DTBPMB (mmol)	Substrate (mmol)	Aniline (mmol)	t (h)	1-oct (%)	Isom (%)	l (%)	b (%)
0.2	0.25	1-octene	11	6	0	0	98	2
0.2	0.25	2-octene	11	6	0	0	97	3
0.2	0.25	4-octene	11	6	0	0	97	3
0.2	0.25	1-hexene	11	3	0	0	99.9	0.1

T= 100 °C, P= 30 bar

No matter what the original position of the double bond was, the products showed very high selectivity to linear amide, since for 1-, 2- and 4-octene the reaction proceeded to completion in 6 hours to afford the linear amide with 97-98 % selectivity. The presence of just one branched product suggests that internal double bonds are not reactive towards carbonylation. Aminocarbonylation of 1-hexene proceeded smoothly to yield the desired linear amide (>99.9 %)

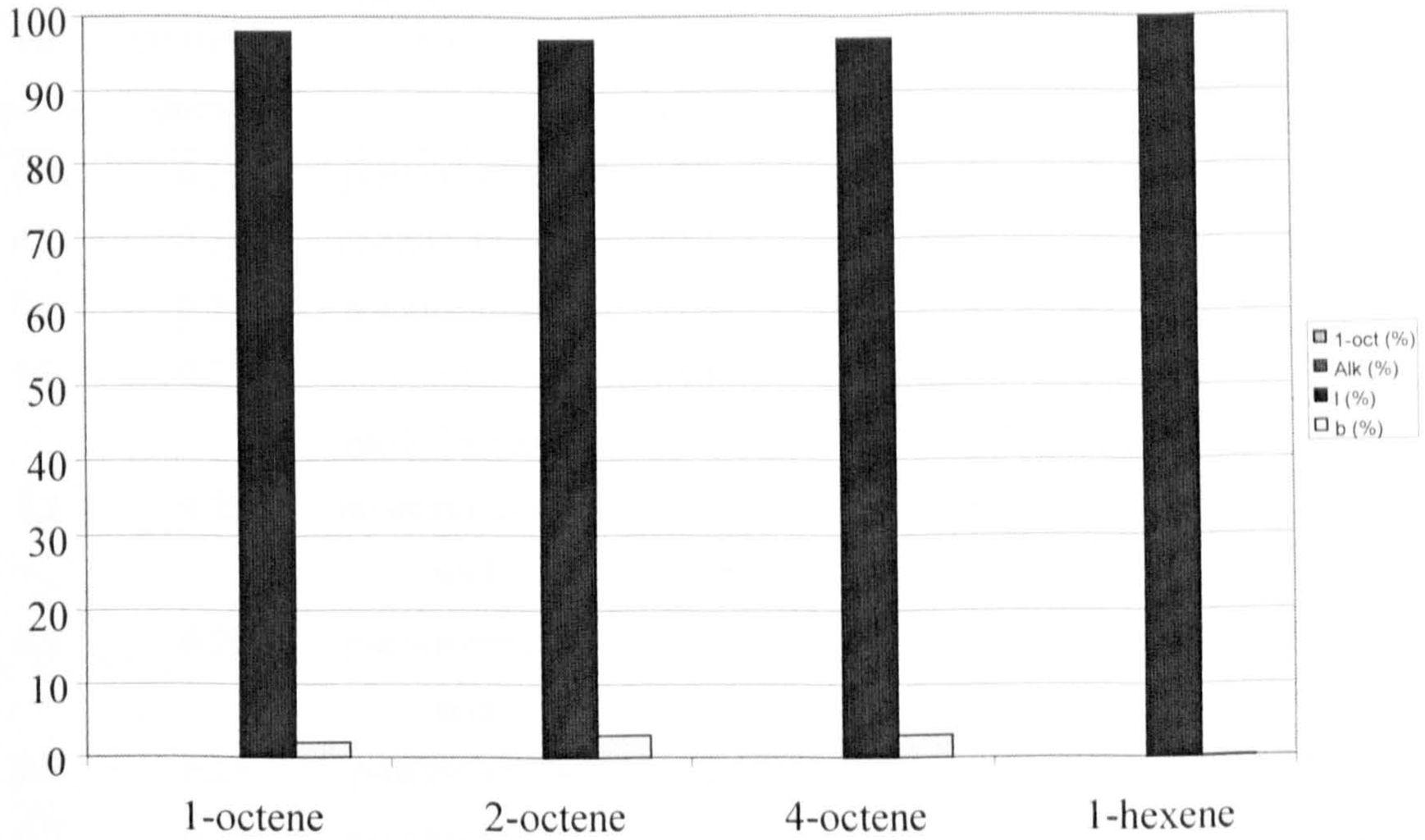


Figure 2-35: Alkenes other than 1-octene

2.3.1.4. Amines other than aniline

In order to gain knowledge of the generality of the reaction, other amines were investigated as the nucleophile. Aromatic amines containing electron donating groups or electron withdrawing groups in *ortho-, meta-* or *para-* positions relative to the amino group were examined. Table 2-23 shows the results obtained.

Ortho-, meta- and *para*-aminotoluene are stronger nucleophiles than aniline, which would favour the attack on the palladium-acyl intermediate. However, the position of the methyl group appeared to have a great influence on the rates and the selectivity of the reaction. The attack of the amino group was sterically hindered by the presence of the methyl group in *ortho-*, whereas if this group was in the *para-* position, the steric effects were minimal (*Figure 2-36*).

Table 2-23: Amines other than aniline

Pd (mmol)	DTBPMB (mmol)	Amine	Amine (mmol)	t (h)	1-oct (%)	Isom (%)	l (%)	b (%)
0.2	0.25	p-aminotoluene	22	3	1	9	80	10
0.2	0.25	m-aminotoluene	22	3	2	30	66	2
0.2	0.25	o-aminotoluene	22	3	5	83	7	5
0.2	0.25	o-amino-methylbenzoate	14	3	7	90	3	0
0.2	0.25	m-aminobenzoic acid	7	3	8	92	0	0
0.2	0.25	p-aminobenzoic acid	7	3	8	92	0	0
0.2	0.25	p-chloroaniline	22	3	4	49	39	8
0.2	0.25	m-chloro-aniline	22	3	0	70	19	11
0.2	0.25	p-amino-anisole	22	3	2	98	0	0

T= 100 °C, P= 30 bar

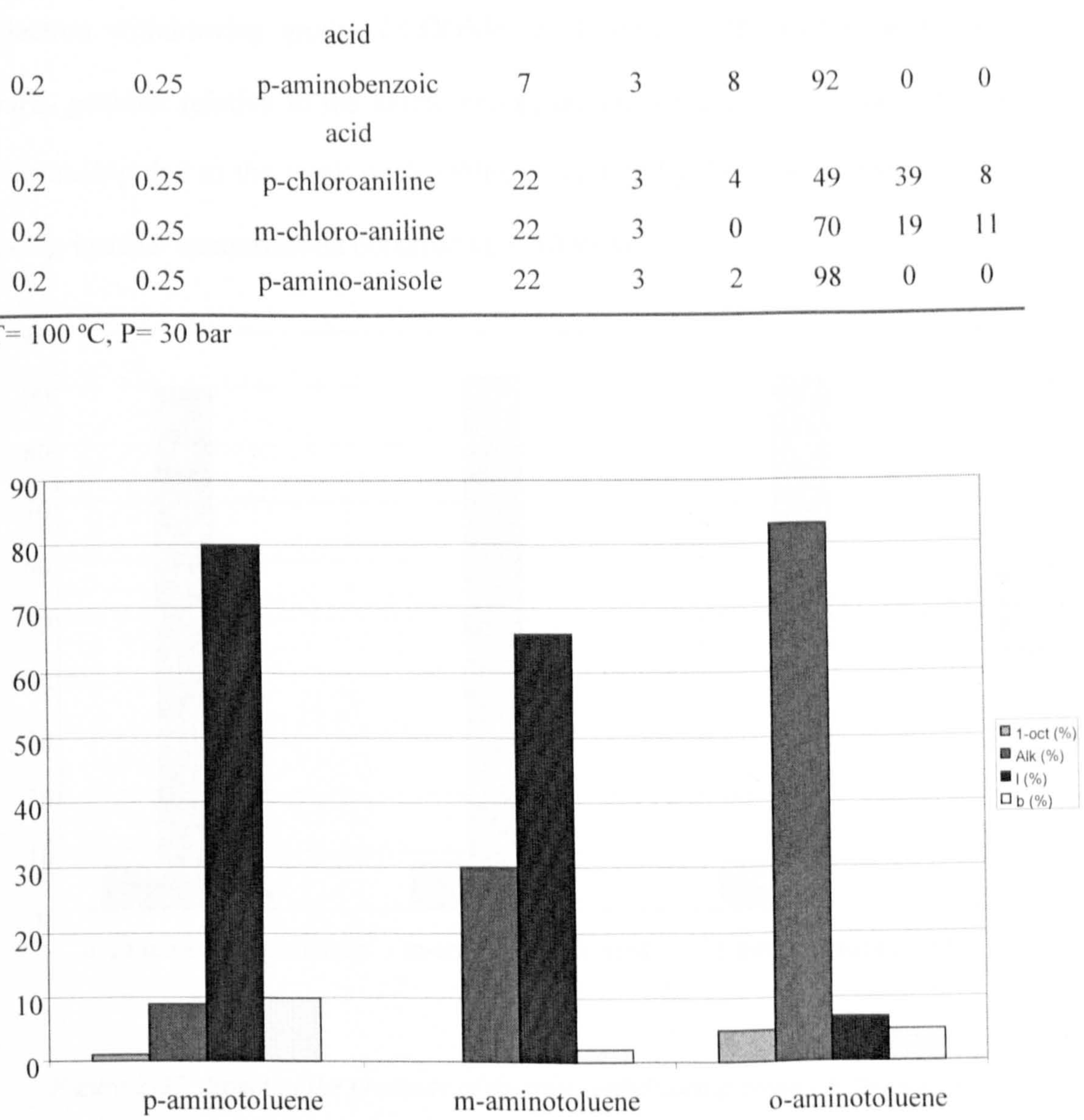


Figure 2-36: Aminocarbonylation of 1-octene with o-,m- and p-aminotoluene as the amine

Due to the lower steric congestion caused by 4-aminotoluene both the conversion or the selectivity to the linear amide were higher than when 3- or 2-aminotoluene were used. The isomerisation decreased correspondingly. However, the branched amide was produced in higher yield in the case of 4-aminotoluene than that of 3-aminotoluene. This may be related to the higher conversion obtained for the former amine.

Electron withdrawing groups (-COOMe or –COOH) in the *ortho-*, *meta-* and *para-* position relative to the amino group, inhibited the carbonylation reaction, presumably due to the weak nucleophilicity exerted by the amino group (*Figure 2-37*); instead isomerisation occurred very effectively.

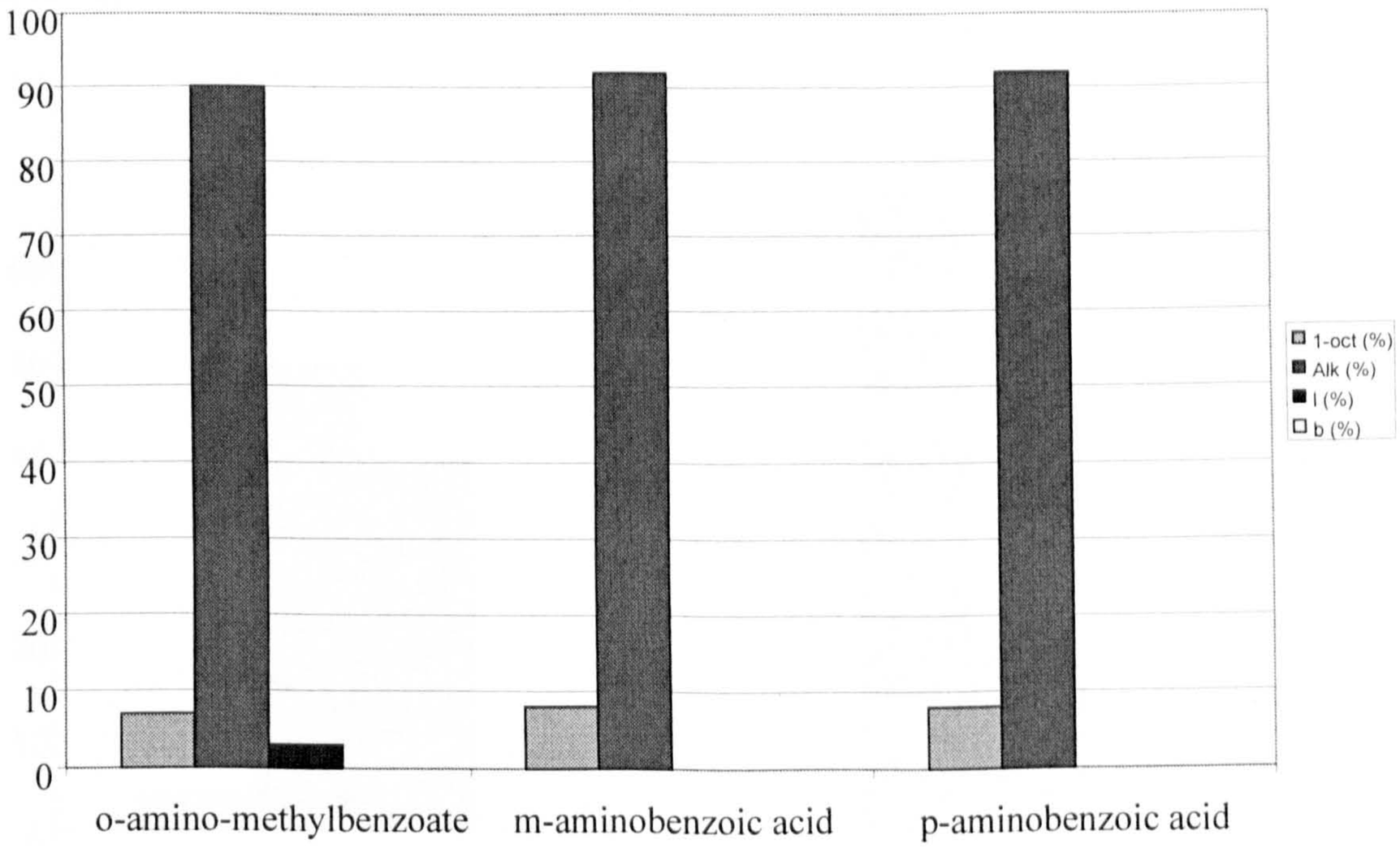


Figure 2-37: Effect of the presence of electron withdrawing groups in the amine.

Other amines studied were 3-chloro-aniline and 4-chloro-aniline. The presence of halogens as substituents in the aromatic ring has two opposite effects: on the one hand they are electron withdrawing by the inductive effect and on the other hand

they are electron donating by the mesomeric effect. We observed that the former appeared to dominate over the latter, making the amino group a weaker nucleophile than in the case of aminotoluenes, whereas the steric effects seemed to control the selectivity (*Figure 2-38*). Thus, the amides corresponding to 4-chloro-aniline were produced in 47 % yield and the linear amide represented 39 % of all the products obtained from the reaction mixture. Isomerisation occurred and internal octenes were produced in 49 % yield. On going from substitution on C_4 to substitution on the C_3 of the ring, isomerisation turned out to be more effective (70 %) in addition to enhance the carbonylation reaction. The branched amide was produced in higher yield when the halogen was in C_3 (11 %) than when it was in C_4 (8 %)

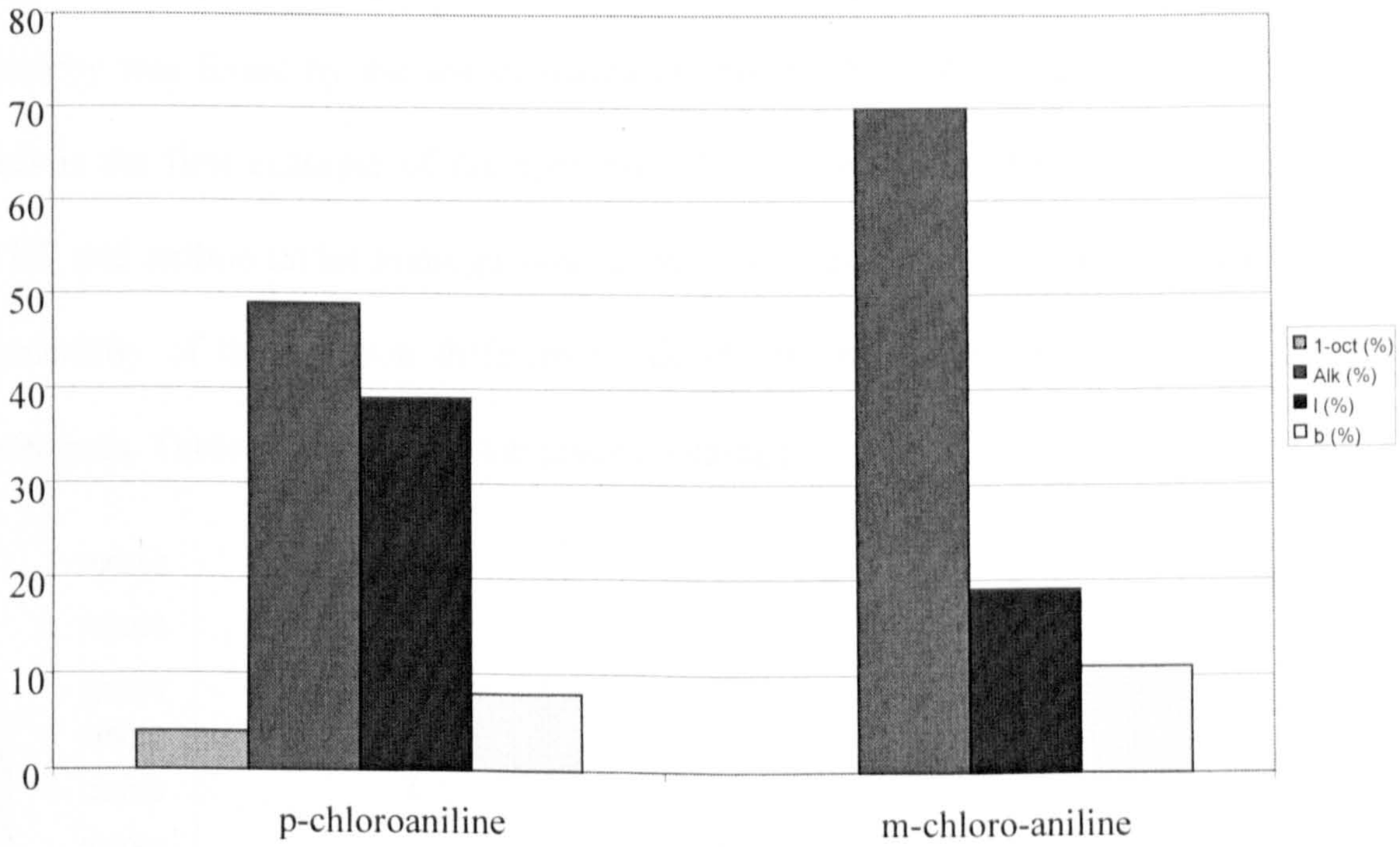


Figure 2-38: Aminocarbonylation of 1-octene with 3- and 4-chloroaniline as the amines

2.4. Aminocarbonylation in THF

The aminocarbonylation of 1-octene was also carried out at 100 °C under 30 bar CO using aniline as the nucleophile in THF as the solvent. Surprisingly, under these conditions not only did 1-octene remain unreacted after 3 hours but also a new product, showing the mass spectrum in *Figure 2-39,* arose. In order to identify this product labelling studies were carried out in d^8-THF. *Figure 2-40* illustrates the mass spectrum obtained. Analysis of the two mass spectra shown clearly reveals that THF is involved in the reaction with aniline. The product was identified as N-phenyl-pyrrolidine (*Figure 2-41 A*). Walkup reported the synthesis of such compounds from a variety of cyclic ethers with primary aromatic amines in 19-77 % yield using an activated alumina catalyst at 270-350 °C.[36] Higher activity was found by the use of titania at 250-300 °C.[37] As far as we are aware this is the first example of the synthesis of N-phenyl-pyrrolidine by reaction of THF and aniline under homogeneous conditions. Therefore, in order to check the generality of the reaction different cyclic ethers and amines were used as the reactants. Table 2-24 displays the results obtained.

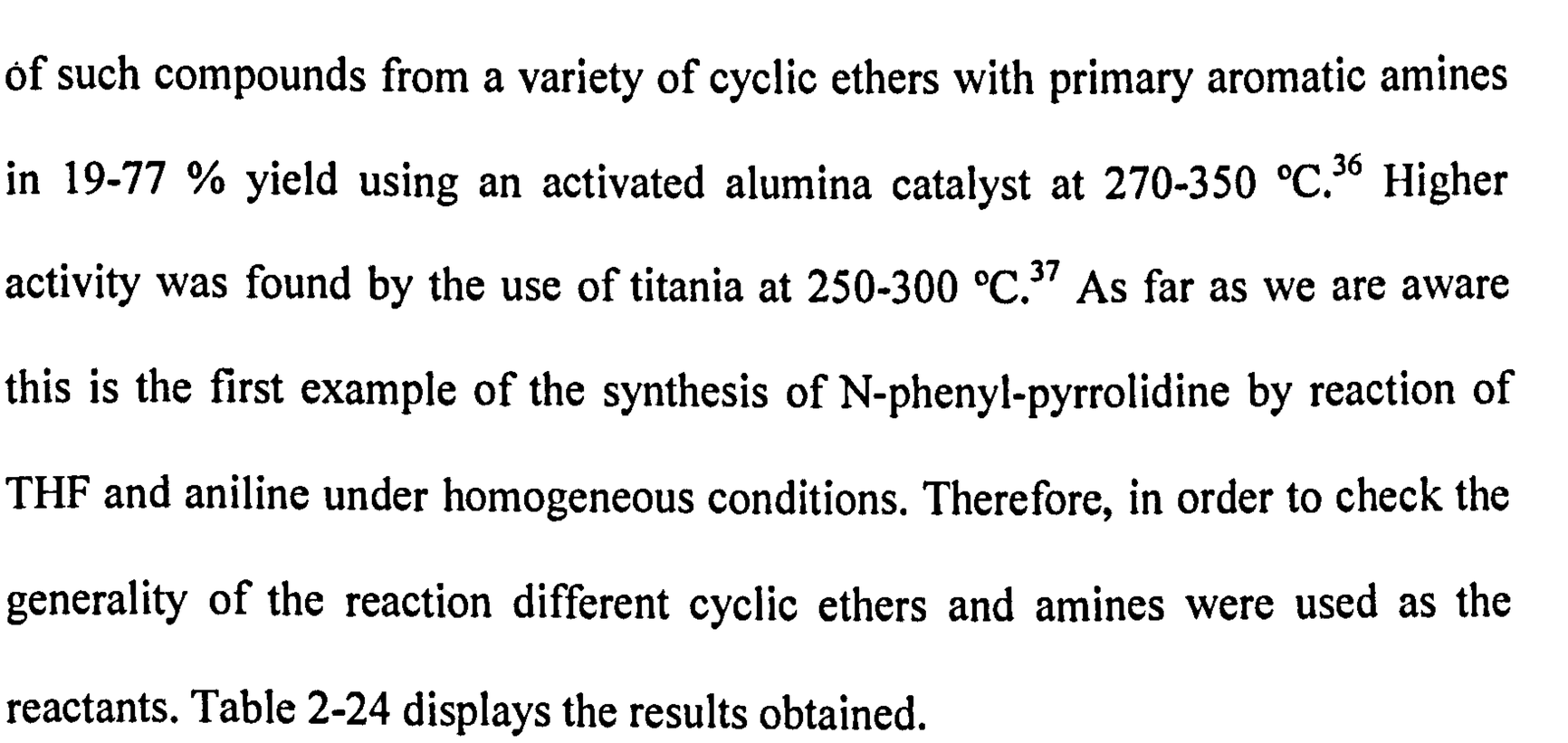


Figure 2-39: Mass spectrum of the product obtained from the reaction of aniline and THF

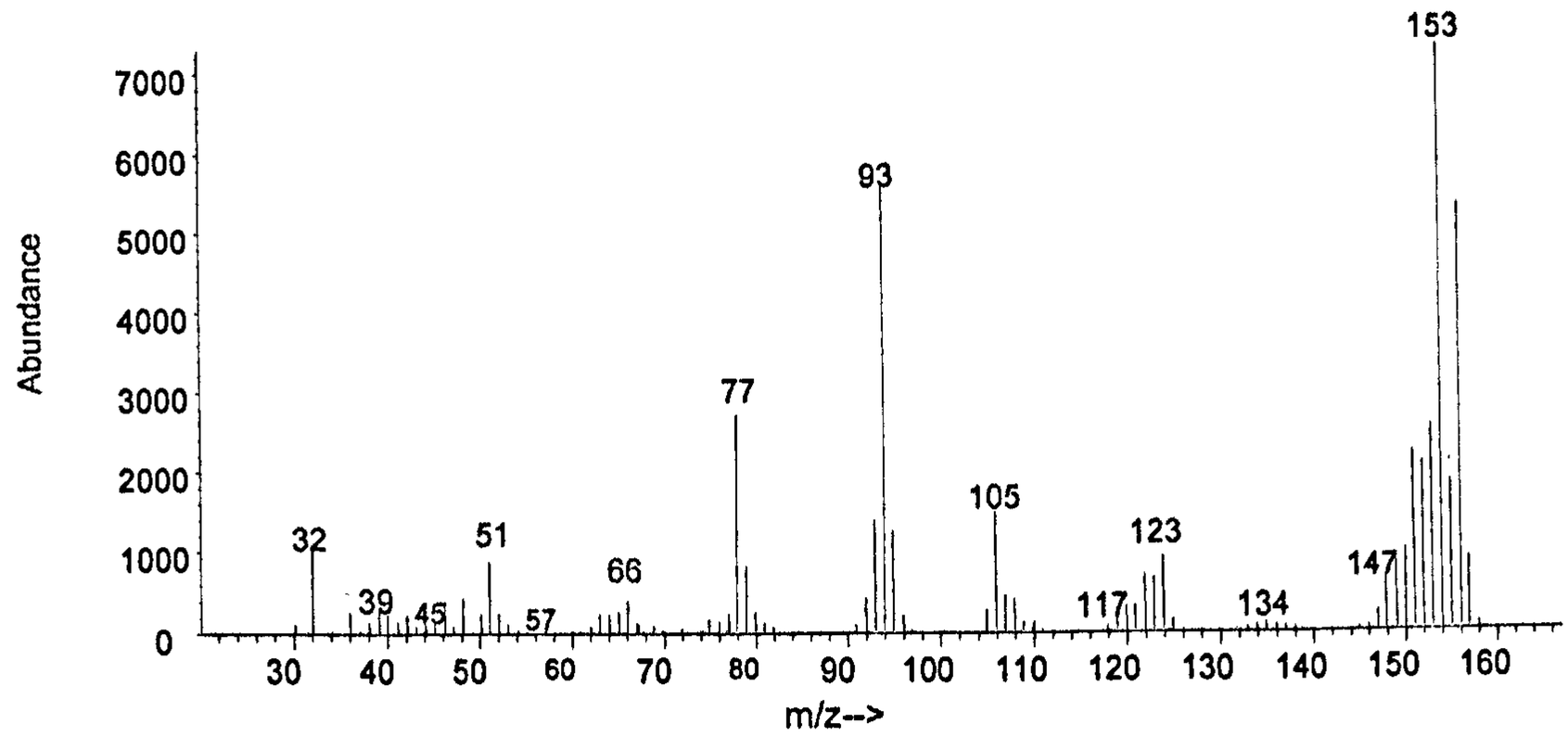
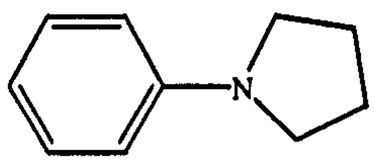


Figure 2-40: Mass spectrum of the product obtained from the reaction of aniline and d^8-THF

Table 2-24: Reaction of amines with cyclic ethers

Pd (mmol)	DTBPMB (mmol)	Substrate	Substrate (mmol)	Solvent	t (h)	Conv (%)
0.2	0.25	Aniline	11	THF	6	25
0.2	0.25	Aniline	11	THF	22	62
0.2	0	Aniline	11	THF	6	0
0.2	0.25	Aniline*	11	THF	6	0
0.2	0.25	Aniline	11	Furan	6	3
0.2	0.25	Aniline	11	1, 4-butyrolactone	6	100
0.2	0.25	Aniline	11	THP	3	< 1
0.2	0.25	Aniline	11	Succinic anhydride/ MeOH	3	32^D, 63^E
0.2	0.25	o-amino-methylbenzoate	7	THF	3	0
0.2	0.25	Octyl amine	11	THF	6	0
0.2	0.25	Cyclohexyl amine	11	THF	6	0
0.2	0.25	Propyl amine	11	THF	6	0
0.2	0.25	Diethyl amine	11	THF	6	4^F

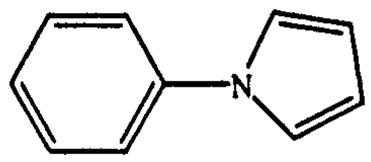
T= 100 °C, P= 30 bar. (*): P_{CO}= 0 bar. (D), (E) and (F): see Figure 2-42.



1-Phenyl-pyrrolidine

(from aniline/ THF)

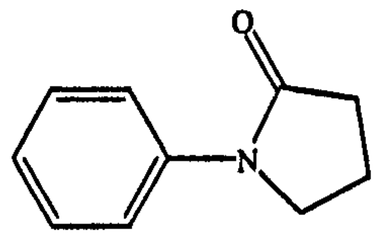
A



1-Phenyl-1*H*-pyrrole

(from aniline/ furan)

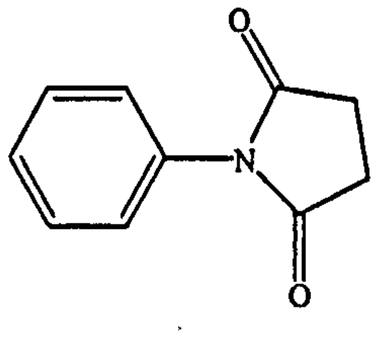
B



1-Phenyl-pyrrolidin-2-one

(from aniline/ 1, 4-butyrolactone)

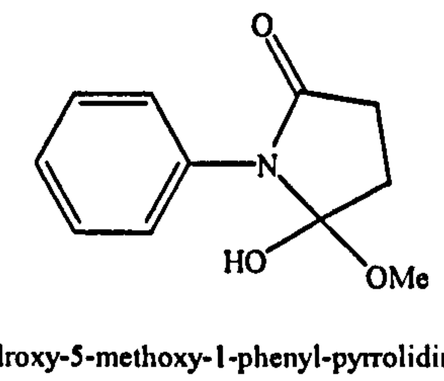
C



1-Phenyl-pyrrolidine-2,5-dione

(from aniline/ succinic anhydride)

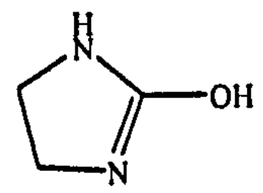
D



5-Hydroxy-5-methoxy-1-phenyl-pyrrolidin-2-one

(from aniline/ succinic anhydride)

E



4,5-Dihydro-1*H*-imidazol-2-ol

(from diethylene diamine/ CO)

F

Figure 2-41: N-phenyl-pirrolidines produced in the reaction between aniline and cyclic ethers.

No reaction occurred in the absence of either DTBPMB or CO, suggesting that the active species in the catalytic cycle contains both of them. Aniline reacted with both saturated and unsaturated cyclic ethers to form the corresponding N-phenyl-pyrrolidine and pyrroles. The reaction between aniline and furan led to the desired product (*Figure 2-41 B*) in very low yield (3 %). N-phenyl substituted lactams are easily produced from lactones and aniline, suggesting that steric hindrance in the cyclic ether is tolerated. N-phenyl-pyrrolidin-2-one (*Figure 2-41 C*) was obtained in 100 % yield using 1, 4-butyrolactone as the cyclic ether. If succinic anhydride was used as the cyclic ether, methanol had to be used as the solvent. Thus, nucleophilic attack of methoxide to the expected product, N-phenyl-pyrrolidine-2,5-dione (*Figure 2-41 D*), occurred to afford the corresponding hemiacetal (*Figure 2-41 E*). The size of the cyclic ether appeared to be limited to five-membered rings, since when tetrahydropyran was used, the respective product was found only in trace amounts. Electron withdrawing groups in the *ortho*-

position of the aniline inhibit the reaction, as observed for 2-amino-methylbenzoate, suggesting that the steric hindrance created in the amine is not allowed. Surprisingly, neither aliphatic amines, nor diamines underwent this reaction to give the corresponding N-alkylation product, suggesting that high electron density on the nitrogen inhibits the reaction.

2.5. Conclusions

In conclusion, we have shown that complexes formed *in situ* from $[Pd_2(dba)_3]$, DTBPMB and methane sulphonic acid provide highly active catalysts for the methoxycarbonylation of terminal alkenes or the tandem isomerisation methoxycarbonylation of internal alkenes to linear carboxylic acid esters. The reactions occur under mild conditions of pressure and temperature *via* a hydride mechanism with rate determining trapping of the acyl species by methanol.

We have also shown that the *in situ* formed complexes from $[PdCl_2]$ and DTBPMB in diethyl ether effectively catalyse the formation of amides from terminal and internal alkenes, carbon monoxide and an aromatic amine. Formation of N-substituted pyrrolidines occurs when this reaction is carried out in cyclic ethers.

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Chapter 3:

METHOXYCARBONYLATION OF ARYL CHLORIDES

3.1. Methoxycarbonylation of aryl chlorides.

The palladium-catalysed carbonylation of aryl halides is a reaction of industrial interest, since a great variety of products, like amides, esters, aldehydes and acids, can be obtained. Aryl halides constitute a very important class of compounds since they are used in C-C coupling reactions among other organic synthesis reactions. Aryl chlorides are cheap, stable, easily prepared and commercially available in a variety of substitution patterns. Due to the low reactivity evidenced by C-Cl bonds high temperatures are required, which usually leads to catalyst decomposition. Carbonylation of aryl chlorides is more difficult than other C-C coupling reactions because a good π-acceptor ligand like CO is present. The effect of CO bound to the palladium centre is to decrease the activity towards oxidative addition and it is also possible for clustering and agglomeration of Pd atoms to occur.

Basset and co-workers reported in 1988 that activation of the C-Cl bond by using $Cr(CO)_3$ favours oxidative addition and therefore carbonylation of aryl chlorides is possible under mild conditions.[1] Two years later, Basset again reported the use of a supported palladium catalyst on activated carbon.[2] Turnover numbers of 5-350 were achieved at 200 °C and 3 bar of CO. In this work they also report the importance of adding an oxidizing agent, like $K_2Cr_2O_7$ or V_2O_5, on the initial rate and total turnover number. These oxidizing agents inhibit the deactivation of the catalyst by oxidation of the particles of metallic palladium to palladium (II) species which can then be reduced under CO to form an active zerovalent palladium complex. Portnoy and Milstein[3] studied the coordination of aryl chlorides to a palladium centre using 1,3-bis(diisopropylphosphino)propane as ligand. They showed that even under a CO atmosphere, the CO-free species

[Pd(η^2-dippp)(η^1-dippp)] is active towards the oxidative addition of PhCl, while the CO-containing species are not. This species loses one phosphine molecule generating a 14-electron complex which undergoes oxidative addition of the aryl chloride.

Alper and co-workers reported the use of a palladium-catalysed carbonylation of haloarenes in the presence of aqueous alkali. They found that iodo and bromobenzene can be carbonylated by [$Pd(PPh_3)_2Cl_2$] under mild conditions using 18-crown-6 ether as phase transfer agent. However, the chloro analogues remained unreactive under the same conditions. Chloroarenes do react at 100 °C with 1 bar of CO in aqueous KOH (20-50 %) in the presence of [$Pd(PCy_3)_2Cl_2$] to give a carboxylic acid. The chloroarene was used as the organic phase and no phase transfer agent was required. Chloroarenes containing electron-donating groups exhibit turnover numbers of 88-116, whereas non-activated chloroarenes achieved a turnover number of 9.[4]

In order to minimize or to eliminate the deactivation of the metal centre very basic ligands, such as 1,3-bis(di-iso-propylphosphino)propane[5] or tricyclohexylphosphine[6], have been used. By using very basic ligands and/ or electron deficient aryl chlorides the electron density at the Pd(0) increases, so the oxidative addition is accelerated. Modification of the palladium complex with these diphosphines leads to carbonylation products, although all yields reported so far are lower than 30 %. In addition, these catalysts are only efficient for highly activated aryl chlorides, i.e., those containing very electron withdrawing groups.

A new catalytic system has been recently reported by Beller.[7] Highly basic phosphines from the group of ferrocenylphosphines are used to modify the palladium precursor. An important advantage of these ligands is their stability in

air and commercial availability. The system requires the presence of a base like sodium carbonate. Activated and non activated aryl chlorides are converted to esters in yields higher than 60 % with more than 80 % selectivity by working at 145°C and less than 5 bar of CO. A turnover number of 1560 was observed for carbonylation of chlorobenzene, which is currently the highest turnover number reported.

Aryl halides are also interesting from the point of view of synthesis of benzoic acids by catalytic hydrocarbonylation. Suzukamo and coworkers[8] have developed a system to form benzoic acid from chlorobenzene. They used $[PdCl_2(PCy_3)_2]$ as catalyst in the presence of a 40 % K_2CO_3 aqueous solution and triethylamine under 5 bar of CO at 180 °C. After 2.5 h, water and ether were added and then 10 % HCl aqueous solution was also added to the reaction mixture. Under these conditions they obtained 97 % selectivity to benzoic acid and a turnover number of 1000. However, no yields are communicated in this paper.

Ziolkowski and coworkers have shown the formation of methyl benzoate in a yield of 90 % from iodobenzene.[9] They report the use of $[PdCl_2(cod)]$ and $[PdCl_2(P(OPh)_3)_2]$ as catalytic precursors in methanol, methanol with $^nBu_4NCl$ and in molten $^nBu_4NCl$ salt. In pure methanol, $[PdCl_2(cod)]$ itself display low activity (5 % yield of methyl benzoate) at 80 °C and 1 bar of CO; however, an increase of the pressure to 5 bar gives 58 % yield to methyl benzoate. Addition of $^nBu_4NCl$ to the reaction mixture counteracts palladium black formation and increases the yield. When the reaction is carried out in molten $^nBu_4NCl$ salt in the presence of a stoichiometric amount of methanol in respect to iodobenzene at 80 °C and 1 bar of CO, the yield increases dramatically to 87 %. Further increase of the pressure to 5 bar gives a yield of 90 %. If the cation in the molten salt is

changed to Me_4N^+ the catalytic activity decreases drastically, giving 8 and 20 % yield under the same conditions as the analogous $^nBu_4N^+$ (87 % and 90 %).

When the reaction was performed with $[PdCl_2(P(OPh)_3)_2]$ at 80 °C and 1 bar of CO, only 13 % of ester was observed. Under 5 bar of CO the yield increased to 63 %. If $^nBu_4NCl$ is used as the molten salt at 80 °C and 1 bar of pressure, 92 % of methyl benzoate was achieved, whereas under 5 bar the yield was 96 %. In the light of the experiments carried out at 1 bar of CO it is concluded that the $[PdCl_2(P(OPh)_3)_2]$ performs differently as in an organic solvent and in molten $^nBu_4NCl$ salt.

Recent work by Indolese[10] appears to improve the reaction conditions for carbonylation of aryl halides. The system chosen to carry out this study was the reaction of 4-bromoacetophenone with CO in butanol in the presence of a base to neutralise the HBr formed. Different solvents and different palladium catalysts were employed. They found the range from 100 to 130 °C to show the best performance, 130 °C being the ideal temperature. To study the rest of the parameters the reaction was carried out at 5 bar CO pressure and 130 °C. Regarding the solvent system, they found neat butanol to give the highest yield (72 %). Surprisingly, if the concentration of butanol was reduced, the yield decreased to 2 %, suggesting that the nucleophilic attack of the anion ^-OBu onto the palladium acyl complex is the rate determining step at low concentration of butanol. The base was the next parameter examined. Trialkylamines gave yields between 50-72 %. Among the trialkylamines studied the largest ones gave slightly lower yield. Inorganic bases like sodium carbonate and sodium acetate led to very poor yields compared to the amines, which was surprising since alkali carboxylates are required for Heck reactions. A comparison between common

$Pd(0)$-PPh_3 and $Pd(II)$-PPh_3 precursor complexes as catalytic precursor is also shown in this work. The former, $[Pd(PPh_3)_4]$, in a concentration of 0.3 mol% turned out to be the most active giving the desired ester in 99 % yield. None of the Pd (II) complexes studied gave a yield higher than 86 %, obtained with 0.1 mol% of $[PdCl_2(PPh_3)_2]$. Even at a concentration of 0.01 mol% of $[Pd(PPh_3)_4]$, this complex was more efficient than $[PdCl_2(PPh_3)_2]$, achieving a turnover number of 6500. However, an increase of the P/Pd ratio to 80 gave a turnover number of 7000, which exceeds all previously reported.

In this chapter the alkoxycarbonylation of aryl chlorides with $PdCl_2$ and DTBMPB in the presence of a base is discussed, stressing the importance of the alcohol on the product distribution and concentrating on the unusual reactivity of 4-chloro-acetophenone and methanol under the reaction conditions used.

3.2. Carbonylation of aryl halides.

3.2.1. Carbonylation of highly activated aryl chlorides.

The palladium precursor was changed from the previous set of experiments from a palladium (0) source to palladium (II) source, like $PdCl_2$, so that acid to oxidise the palladium from oxidation state 0 to oxidation state II is no longer needed. In addition the chlorine present in the substrate and in the palladium precursor would form HCl with the protons coming from the methanol, so base was required to neutralise the solution.

To gain a greater understanding of the activity of this catalytic system for the methoxycarbonylation of aryl chlorides, 4-chloro-methylbenzoate, 4-chloro-nitrobenzene and 4-chloro-cyanobenzene were studied as the substrates. Having highly electron withdrawing groups in the *para-* position relative to the chlorine, these compounds are highly activated towards nucleophilic aromatic substitution.

Using KO^tBu as the base, methoxycarbonylation of 4-chloro-methylbenzoate to afford the expected dimethyl terephthalate occurred in 16.4 % yield. However, two other major products were produced: 4-methoxymethylbenzoate in 22.6 % yield and methylbenzoate in 24.2 % yield. The formation of these products may be related to the strength of the base, since it could abstract the chlorine and then facilitate further reactions on the ring. The formation of 4-methoxymethylbenzoate suggests that nucleophilic aromatic substitution, which requires harsh conditions, is possible under these conditions. In order to confirm the influence of the base, the reaction was performed in the presence of NEt_3. The use of NEt_3 instead of $KOBu^t$ led to an increase in the catalyst efficiency. However, in both cases palladium black was found at the end of the

reaction. Methoxycarbonylation was significantly more selective and the side-reactions which occurred in the previous case were supressed, since only dimethyl terephthalate was produced in 35 % yield after 18 hours. Slight reaction (4 %) was observed after 48 hours in the absence of base.

If instead of methanol 2, 2, 2-trifluoroethanol (TFE) was used as the solvent (*Figure 3- 1*), the desired asymmetric diester was produced in 90 % yield, whereas the transesterification product was formed in 7 % yield. Alkoxycarbonylation of non activated chlorobenzene with TFE afforded the desired product in 20 % yield.

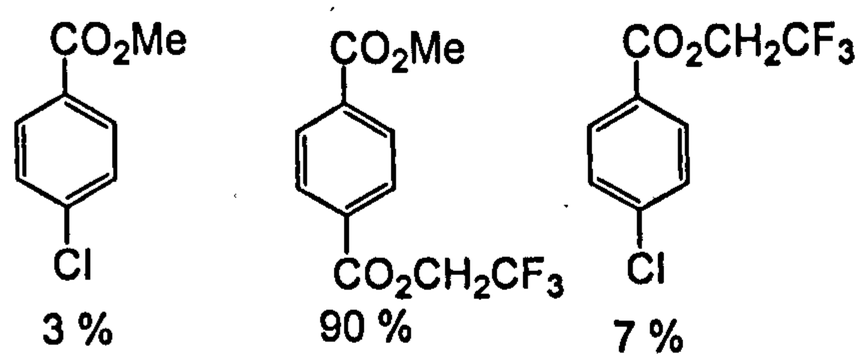


Figure 3- 1: Alkoxycarbonylation of 4-chloro-methylbenzoate with TFE.

Methoxycarbonylation of 4-chloro-benzonitrile provided a mixture of products. *Figure 3- 2* depicts the products formed and the yields obtained. The major product was obtained from displacement of the cyanide by methoxide. Most of the compounds produced contained a –COOMe group, which may arise from a catalytic reaction or from the competitive hydrolysis of the nitrile group followed by esterification. Nevertheless, *p*-cyano-methylbenzoate and dimethyl terephthalate are formed by metal-catalysed processes. The former is the expected product from this reaction, in which the chlorine has been replaced by an acetate group and the nitrile group remains in the same position. However, the latter may be formed either by hydrolysis-esterification of 4-nitrile-methylbenzoate or carbonylation of 4-chloro-methylbenzoate. The presence of

methoxy groups instead of chlorine suggests that nucleophilic aromatic substitution also occurs.

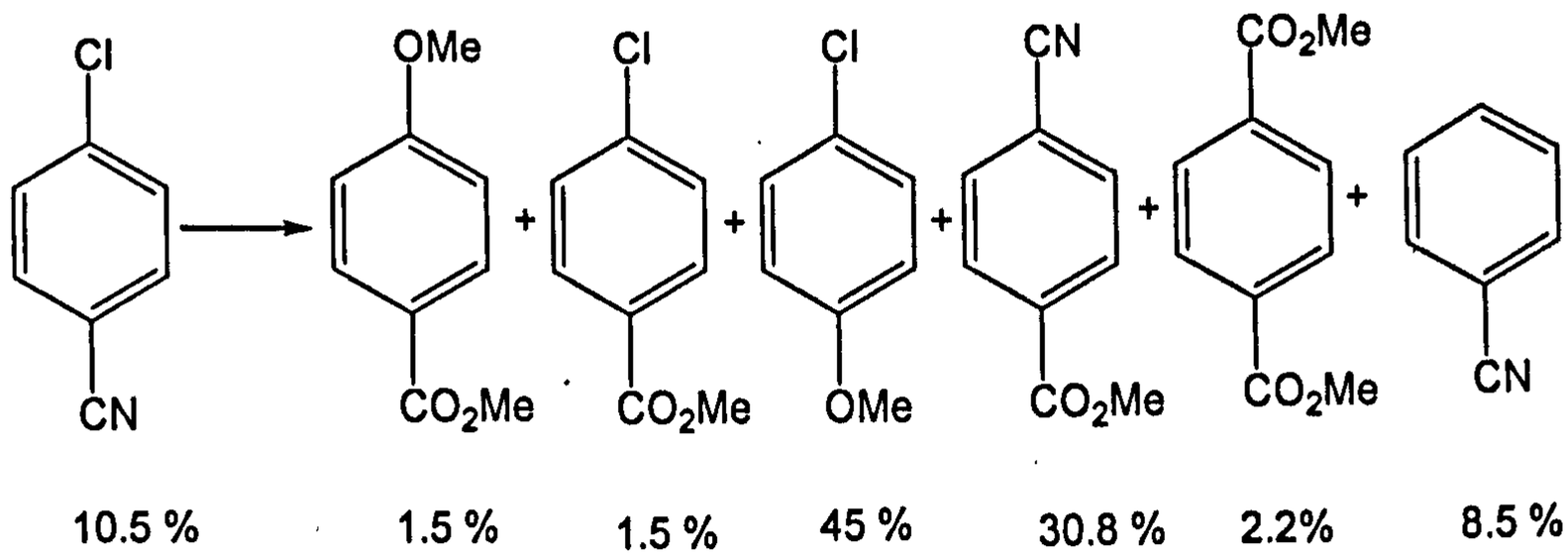


Figure 3- 2: Methoxycarbonylation of p-chloro-cyanobenzene.

The methoxycarbonylation of 4-chloronitrobenzene led to the formation of several products (*Figure 3- 3*) related to those obtained with 4-chloro-methylbenzoate. The reduction of the nitro group resulted in the formation of aniline, which underwent carbonylation to afford anilides (-NHCHO groups) and carbamates (-$NHCO_2R$ groups). Formation of carbamates from nitroaromatic compounds is well known[12, 13, 14, 15, 16]; however, to the best of our knowledge, this synthesis of anilides is unprecendented. Nucleophilic aromatic substitution of the chlorine by the methoxy group occurred very effectively. Surprisingly, the expected 4-nitromethylbenzoate was not formed.

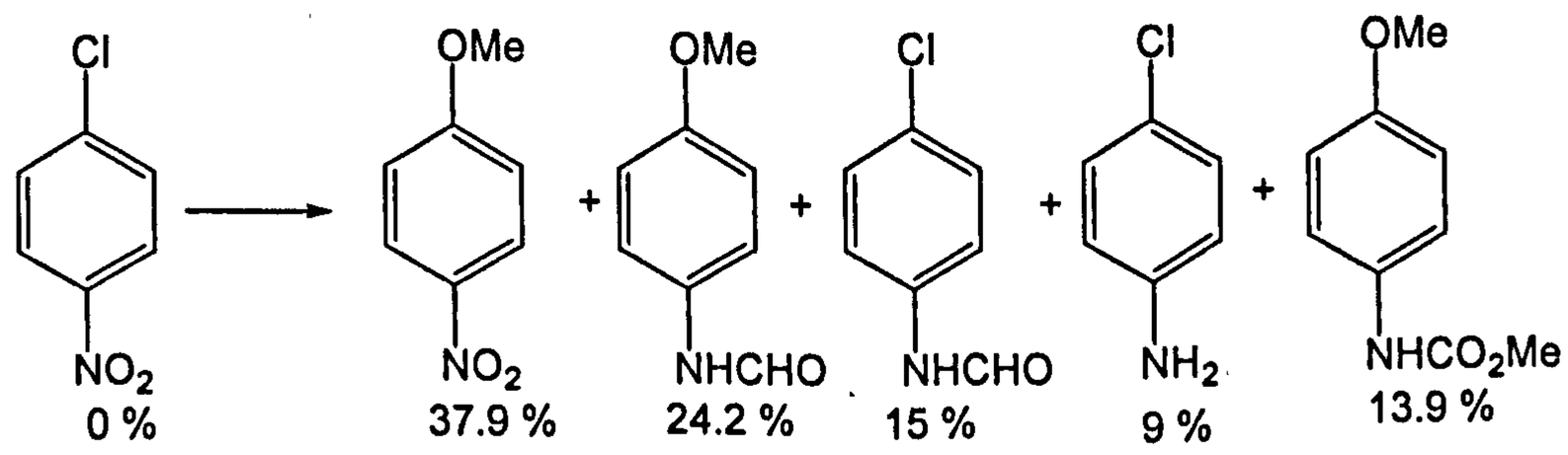


Figure 3- 3: Methoxycarbonylation of 4-chloro-nitrobenzene.

The carbonylation of the nitro group to give the carbamate group occurred. However, a methoxy group was found in the *para-* position instead of the expected chlorine. This suggests that the nucleophilic aromatic substitution is

fast compared to the carbonylation reaction, since otherwise the chlorine could not have been substituted due to the deactivating effect of the carbamate group. The formation of anilides can be explained by analogy with the mechanism operating when ruthenium is the metal centre employed[11]. Aromatic isocyanates are used on a large scale for the production of polyurethanes. Normally, the starting materials to produce aromatic isocyantes are the corresponding nitro compounds. These are then hydrogenated to yield an amine, which is subsequently reacted with phosgene to get the desired polyurethanes. The research in this field has been focused in developing a system capable of producing polyurethanes without the phosgene step. Consequently, the homogeneous catalytic carbonylation of nitroaromatics has focused the interest of many industries and research groups for more the 30 years. There are numerous patents[21,22] and publications[23,24] which report the direct formation of aryl isocyanates from carbonylation of nitroaromatics (*Equation 3-1)*:

$$Ar\text{-}NO_2 + 3\ CO \longrightarrow Ar\text{-}NCO + 2\ CO_2$$

Equation 3-1: Formation of aromatics isocyanates from nitroaromatics

Nevertheless, the lifetime of the catalysts used is very low, besides not being able to carbonylate nitroaromatic compounds. A way of modifying these catalysts was by addition of an alcohol like methanol. In this case the product obtained would be a carbamate[25,26,27,28,29,30] (*Equation 3-2*). This is then turned into the desired isocyanate by removal of the methanol at high temperature. Ruthenium carbonyls have been used successfully as catalysts for the carbonylation step at pressures of 60 atm and temperatures of 150 °C.

$$Ar\text{-}NO_2 + 3\ CO + MeOH \longrightarrow Ar\text{-}NHC(O)OMe + 2\ CO_2$$

Equation 3- 2: Formation of aromatic carbamates from nitroaromatics.

We propose the following mechanisms to be operating in the formation of all this products (*Figure 3- 4*).

Formation of p-chloro-aniline and thep-chloro-benzocarbamate.

The first step in the mechanism to forming a direct bond between the metal and the nitroaromatic involves loss of carbon dioxide and decoordination of one of the phosphorous of the ligand to become unidentate (species 2). Coordination of CO facilitates the formation of a metal-nitrosoarene (species 3). Further expulsion of CO_2, recoordination of the ligand as bidentate and migration of the hydride from the metal to the nitrogen atom lead to the formation of species 4, which in the presence of methanol releases *p*-chloro-aniline and forms a palladium-methoxide (species 5). Insertion of CO into the palladium-methoxide bond affords species 6, which undergoes nucleophilic attack of *p*-chloro-aniline producing the initial palladium-hydride (species 1) and the carbamate.

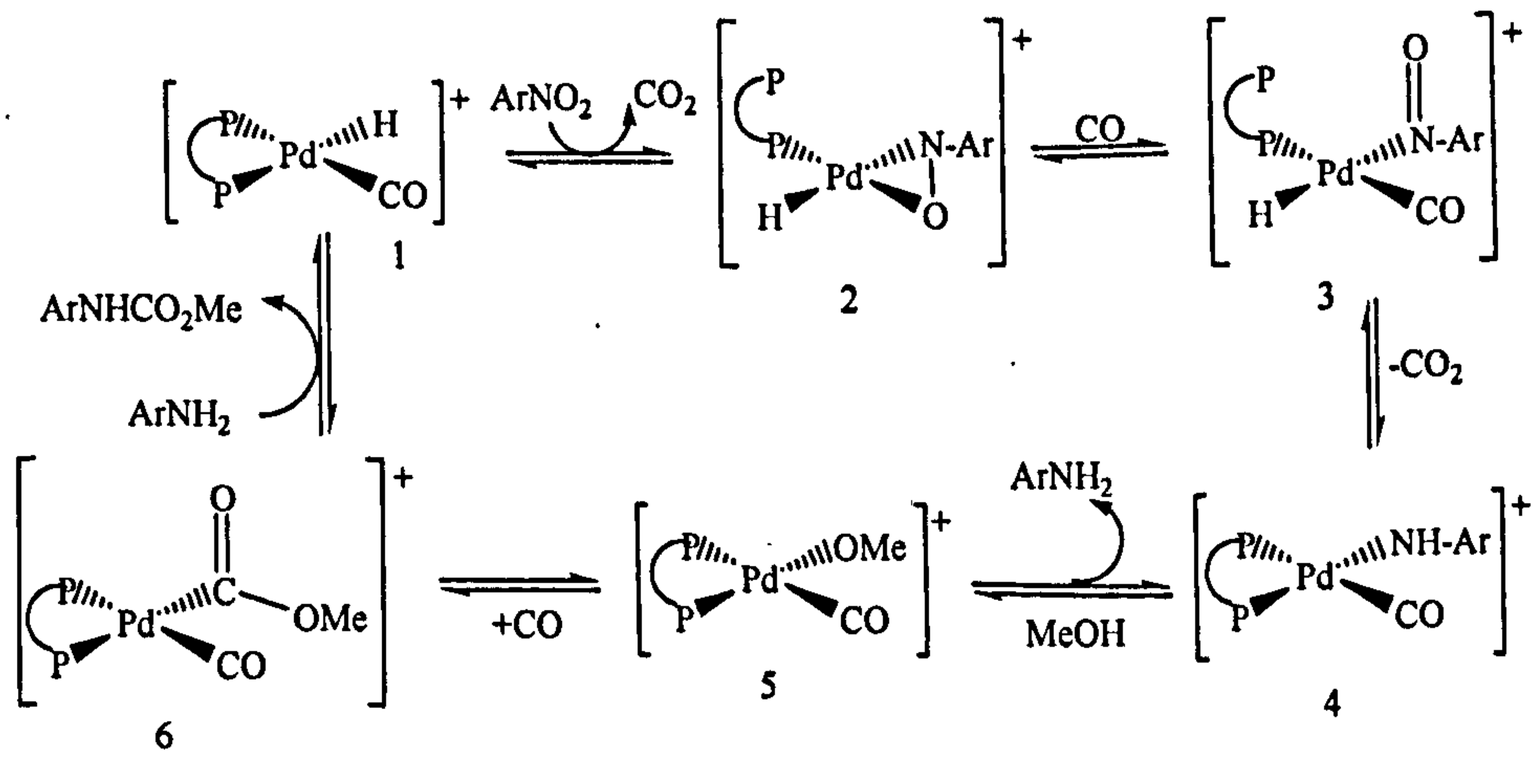


Figure 3- 4: Formation of p-chloroaniline

Formation of p-chloroformanilide

This way of producing *p*-chloroformanilide has not been reported. We proposed the following mechanism to be operating (*Figure 3- 5*). In the methoxy carbonyl palladium complex, replacement of the methoxy ligand by the aniline could occur to lead to a palladium (II) intermediate. The next step would be the CO

insertion into the palladium-nitrogen bond leading to a -CONHAr ligand. At this stage methanol is critical again for protonation to give the hydrido dication. The final step involves the reductive elimination of the hydride carbamyl regenerating the palladium (II) species and releasing 4-chloroformanilide.

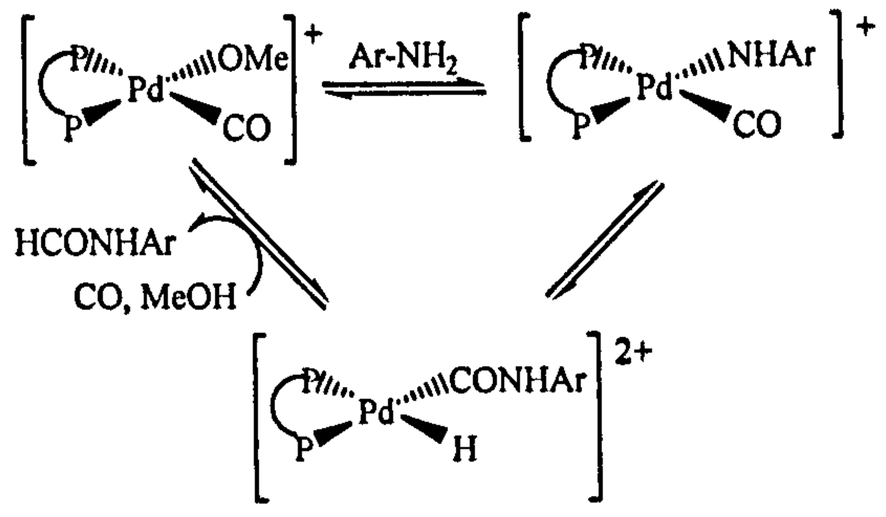


Figure 3- 5: Formation of 4-chloroformanilide.

3.2.2. Carbonylation of moderately activated aryl chlorides.

Based on these results, we next examined the reactivity of 4-chloroacetophenone, which has a weaker electron withdrawing group in the position *para-* to the chlorine, towards methoxycarbonylation to yield 4-acetylmethylbenzoate. In the first attempt the reaction was carried out using $KOBu^t$ as the base. Surprisingly, a mixture of seven products (one of which unidentified) was obtained; however, the direct methoxycarbonylation product was not observed (*Figure 3- 6*).

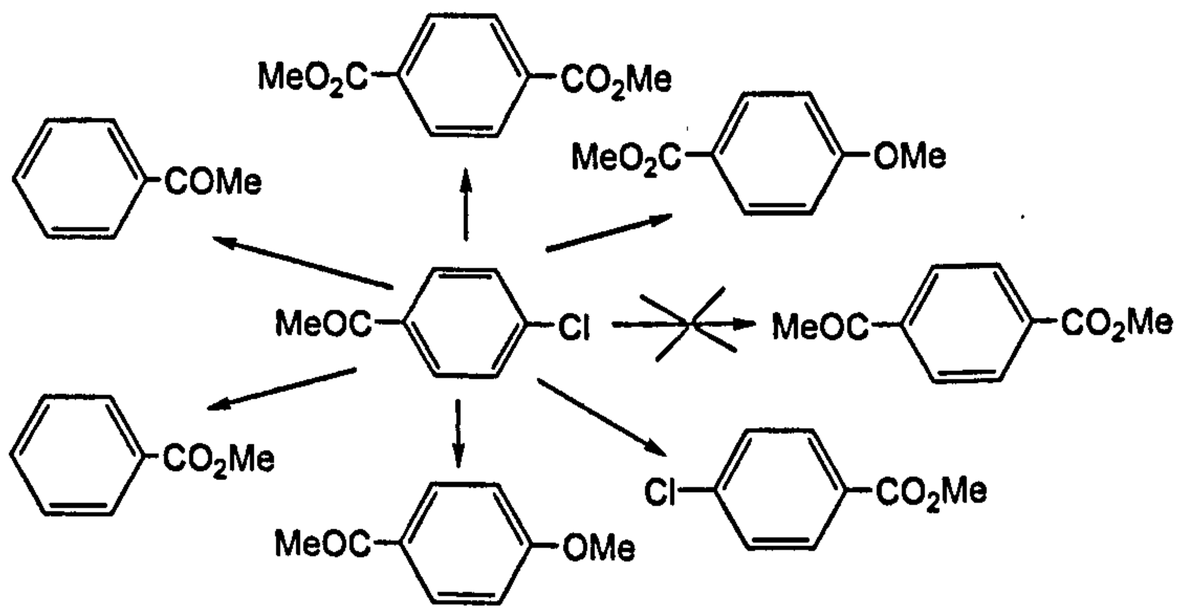
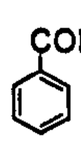
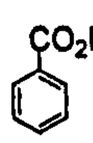
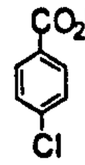
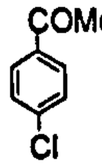
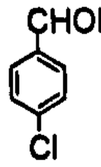
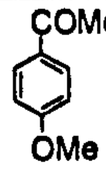
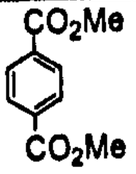


Figure 3- 6: Mixture of products observed in the methoxycarbonylation of 4-chloroacetophenone.

Interestingly, after 24 hours the reaction had hardly started (only 24.5 % conversion had been achieved). Attempts to make it go to completion increasing the reaction time to 48 and 56 hours were unsuccessful. The performance of the catalyst at 80 °C and 100 °C was also examined. Table 3- 1 lists the products observed and their yields.

Table 3- 1:Influence of temperature and reaction time.

T (°C)	t (h)								unknown
100	24	2.1	0	7.8	75.5	0.8	8.8	3.5	1.5
100	48	1.1	1.5	21.1	36.6	1.1	20.9	16.6	1.1
100	56	8.8	3.6	24.8	14	2.9	22.4	20.4	3.2
80	48	0	0	27.7	57.5	0	8.7	0	6.1

At 100 °C 36.6 % of 4-chloroacetophenone remained after 48 hours. The major product was 4-chloro-methylbenzoate (21.1 %) and dimethyl terephthalate was formed in 16.6 %, whereas at 80 °C 4-chloro-methylbenzoate was formed in a 27.7 % yield and no dimethyl terephthalate was produced, suggesting that (1) 4-chloroacetophenone is first converted into 4-chloromethylbenzoate and this undergoes methoxycarbonylation to afford dimethyl terephthalate and (2) the activation energy for the methoxycarbonylation of 4-chloromethylbenzoate to occur is higher than that for its formation from 4-chloroacetophenone. Degradation of the starting material and 4-chloro-methylbenzoate by loss of chlorine afforded acetophenone and methylbenzoate. At 80 °C the yields obtained for all the products were lower than at 100 °C, except in the case of 4-chloromethylbenzoate. It is also noteworthy that nucleophilic aromatic substitution of chlorine by methoxide and the conversion of the methyl ketone

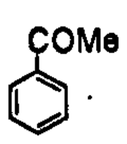
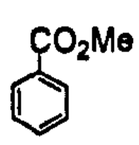
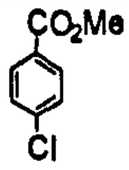
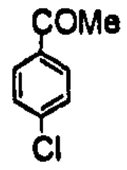
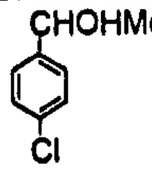
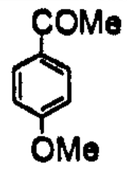
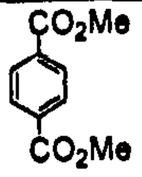
into a methyl ester are fast compared with the remaining transformations occurring during the reaction.

In order to reduce the number of products formed, different reaction conditions were investigated and the results obtained are shown in the following sections.

3.2.2.1. Effect of the base.

The choice of the base is crucial since its role is not only to neutralise the HCl formed *in situ* but also to produce the alkoxide anion which attacks the palladium acyl complex. Common organic and inorganic bases of different strength have been studied (Table 3- 2). In the presence of triethylamine dimethyl terephthalate was produced selectively and in 38.3 % yield. If an inorganic base like KOH was used, acetophenone was obtained in 60 % yield as the major product, whereas dimethyl terephthalate was produced in 29 % yield, suggesting that 4-chloromethylbenzoate is formed and consumed rapidly and that dehalogenation becomes competitive with the formation of the esters. According to the data compiled, weak bases appear to be most selective in the carbonylation reaction, suggesting that strong bases are required for nucleophilic aromatic substitution and dehalogenation to occur. However, even in the absence of base the reaction takes place, although to low conversion, since the formation of the nucleophile MeO^- is slower.

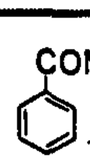
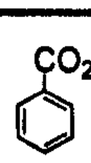
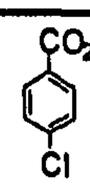
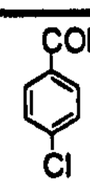
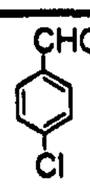
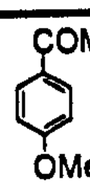
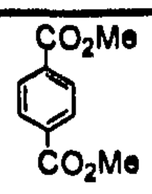
Table 3- 2: Influence of the base

									unknown
Base	$KOBu^t$	1.1	1.5	21.1	36.6	1.1	20.9	16.6	1.1
	NEt_3	0	0	0	58	0	0	38.3	3.7
	KOH	60	0	0	0.9	2.1	4	29	4
	No base	0	0	0	87	0	0	11	2

3.2.2.2. Effect of the presence of CO.

In order to gain an understanding of how the reaction of formation of 4-chloro-methylbenzoate and dimethyl terephthalate proceeds (*via* methoxycarbonylation or *via* organic chemistry reactions), the role of CO was investigated (Table 3- 3). In the absence of CO no starting material was recovered at the end of the reaction. However, products formed *via* transfer hydrogenation were found in >50 % yield. Nucleophilic aromatic substitution of chlorine by the methoxy group also occurred affording 4-methoxyacetophenone in 19.4 % yield. Neither 4-chloromethylbenzoate nor dimethyl terephthalate were produced under these conditions. The absence of esters suggests that CO is involved in the replacement of the ketone by an ester function. It is interesting that even in the absence of both CO and base small amounts of acetophenone were formed, but neither nucleophilic aromatic substitution nor carbonylation reactions occurred.

Table 3- 3: Influence of the presence of CO

P_{CO} (bar)								unknown
20	1.1	1.5	21.1	30.7	1.1	20.9	16.6	1.1
0[1]	14.5	0	0	0	17.3	19.4	0	0
0[2]	11	0	0	78.5	0	0	0	10.5

[1] 1-hydroxyethylbenzene (33.4 %), phenylpropanone and phenylbutanone (8.5 %), 1-methoxy-2-methylanisole (6.9 %). [2]No base present

Knowing that CO is required for the formation of the two esters, we investigated which processes are catalysed by palladium-DTBPMB complexes and which are just organic reactions, by performing the methoxycarbonylation with and without the palladium/DTBPMB.

3.2.2.3. Effect of the catalyst.

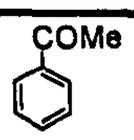
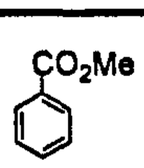
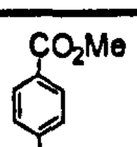
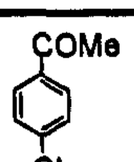
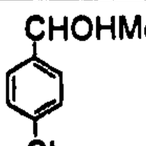
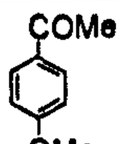
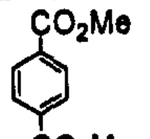
Given all the compounds formed throughout the reaction, we suspected that not all of them would be metal catalysed products. Therefore, some experiments were carried out in the absence of the catalytic system (Table 3- 4).

No esters were produced either in the absence of catalyst, base and CO pressure or in the presence of catalyst but in the absence of both CO and $KOBu^t$. The product from nucleophilic aromatic substitution, 4-methoxy-acetophenone, was not observed either when CO and $KOBu^t$ were absent. However, in the presence of just $KOBu^t$ 4-methoxy-acetophenone was the major product (88 %), suggesting that nucleophilic aromatic substitution is very effective only when this base is present. In the presence of CO and $KOBu^t$ but in the absence of catalyst 4-chloro-methylbenzoate was produced (22.5 %) proving that only base and CO are involved in the transformation of the ketone into an ester. However, no dimethyl terephthalate was detected, confirming that dimethyl terephthalate is

not produced from direct methoxycarbonylation of 4-chloroacetophenone but by tandem formation-methoxycarbonylation of 4-chloromethylbenzoate and that palladium-DTBPMB complexes are required in the last step.

These findings led us to conclude that only the formation of dimethyl terephthalate is metal-catalysed (*Figure 3- 7*). In addition, we could also confirm that the catalyst is involved only in the formation of one of the two ester groups, whereas in the other one the carbonyl remains from the 4-chloroacetophenone.

Table 3- 4: Effect of the catalyst.

KO^{t}Bu	P_{CO} (bar)	Cat								unknown
Yes	20	Yes	1.1	1.5	21.1	30.7	1.1	20.9	16.6	1.1
Yes	0	Yes[a]	14.5	0	0	0	17.3	19.4	0	0
No	0	Yes	11	0	0	78.5	0	0	0	10.5
Yes	20	No	2.2	0	22.5	55.6	3.2	16.5[b]	0	0
Yes	0	No	6.8	0	0	1.5	3.3	88	0	0

[a] 1-hydroxyethylbenzene (33.4 %), phenylpropanone and phenylbutanone (8.5 %), 1-methoxy-2-methylanisole (6.9 %). [b] *p*-methoxyacetophenone and *p*-methoxymethylbenzoate could not be separated.

Knowing the role of the base and of the CO and which reaction is catalysed by Pd-DTBPMB complexes, there were still two unsolved questions: (1) are the two methoxy containing products formed by nucleophilic aromatic substitution or *via* a benzyne intermediate, and (2) is the dimethyl terephthalate formed by oxidation of the aceto group or formal nucleophilic displacement of CH_3^- by OCH_3^-. In order to answer these questions, mechanistic studies on the methoxycarbonylation of 4-chloroacetophenone have been carried out and the results will be discussed in section 3.2.2.5.

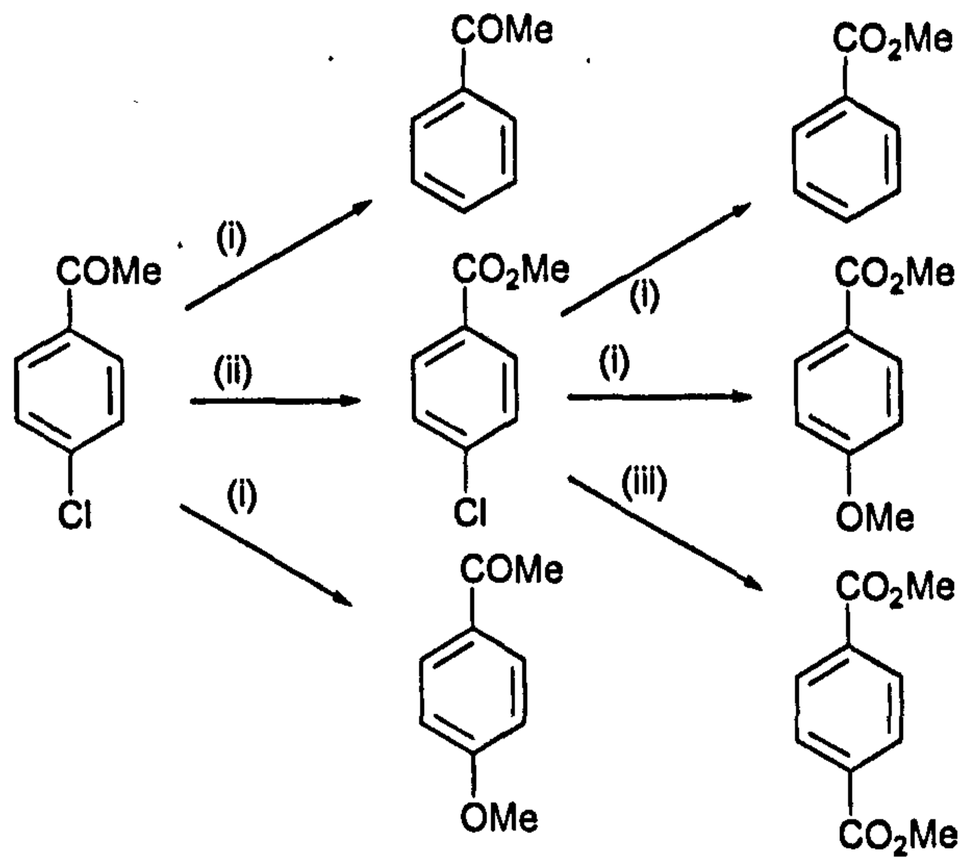
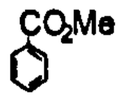
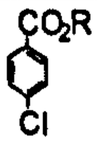
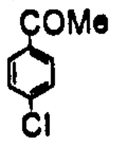
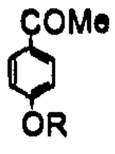
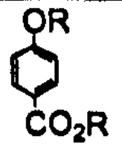
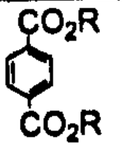
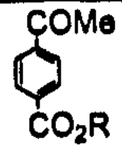


Figure 3- 7: Products from the methoxycarbonylation of 4-chloroacetophenone and their origins. (i) KOBu^t, MeOH; (ii) CO, KOBu^t, MeOH; (iii) Pd/DTBPMB, CO, KOBu^t, MeOH.

3.2.2.4. Other primary alcohols.

To examine the generality of the alkoxycarbonylation of 4-chloroacetophenone and especially to attempt to reduce the formation of side products and to gain understanding on the mechanism, the reaction was carried out using primary alcohols (2, 2, 2-trifluoroethanol (TFE) and *n*-propanol) other than methanol (Table 3- 5). Therefore, a relationship between steric hindrance, nucleophilicity and reactivity could be established. The nucleophilicity order for these alcohols is n-PrOH>MeOH>TFE, whereas according to the steric bulk the order is n-PrOH>TFE>MeOH. Thus, nucleophilic aromatic substitution and nucleophilic attack on the acyl intermediate were expected to proceed faster in n-PrOH than in the other alcohols.

Table 3- 5: Different alcohols

Alcohol								
MeOH	3.5	1.2	12.8	48.5	1.5	13.8	10.8	0
n-PrOH	0	0	20	20	1.8	1.1	19	38
CF_3CH_2OH	0	0	4	0	0	0	6	90

Alkoxycarbonylation was successfully initiated in both of these alcohols. However, MeOH appeared to promote a larger number of reactions, the reactivity order being MeOH>PrOH>TFE. Therefore the steric effects are critical at this stage and it is important to find a compromise between the electronic and steric properties of the alcohol. A methoxy group is able to approach the aromatic ring more effectively and therefore can easily attack and substitute the chlorine. Nevertheless, an outer-sphere attack of alkoxide ions has been discussed as a possible mechanism for this reaction, which typically occurs in highly basic media, where the nucleophile is the alkoxide anion. Yamamoto and coworkers reported that aryl acetates were formed by the intramolecular process of reductive elimination from (aryloxy)(acetyl)-palladium complexes.[16]

The use of either n-propanol or TFE provided the new products, 4-acetyl-(2,2,2-trifluroethyl)benzoate (*Figure 3- 8*) and 4-acetyl-propylbenzoate (*Figure 3- 9*). The case of the less nucleophilic, TFE, was especially successful because not only did it hinder the formation of both 4-chloroalkylbenzoate and the diester but also products arising from non-carbonylative ring dechlorination, which promotes the alkoxycarbonylation reaction. Moreover, the reaction proceeded smoothly to completion to afford the desired product in 90 % yield, along with 4 % yield of 4-chloro-2,2,2-trifluoroethylbenzoate and 6 % yield of 1,4-benzenedioic acid bis-(trifluoroethyl) ester (*Figure 3- 8*). The lack of formation of any nucleophilic

aromatic substitution product when TFE was the solvent was a remarkable observation, emphasising the need of a strong nucleophile to carry out nucleophilic aromatic substitution. Surprisingly the yield of p-acetyl-alkoxybenzoate decreased on going from TFE to *n*-propanol: 90 % and 38 % respectively. These results suggest that less nucleophilic alcohols are required to produce the desired alkoxycarbonylation product in high yield.

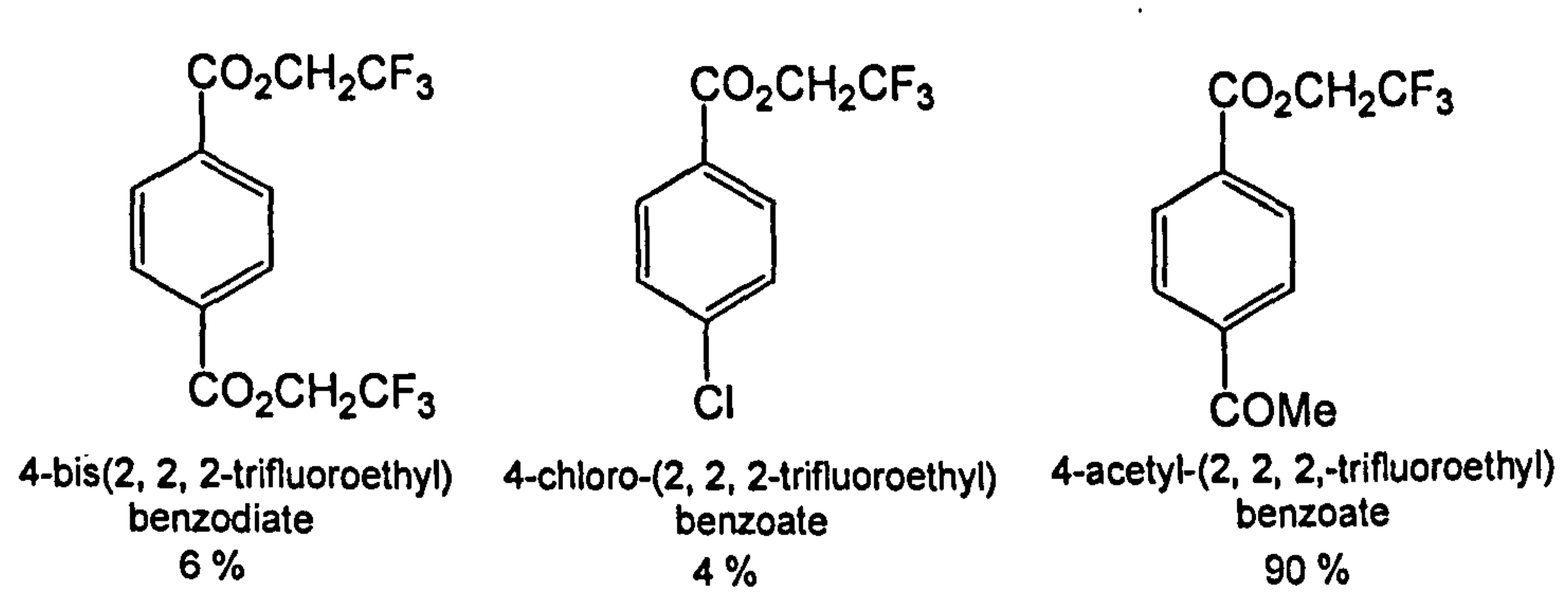


Figure 3- 8: Structure of the products obtained in the alkoxycarbonylation with (2,2,2)-trifluoro-ethanol

In n-propanol the reaction led, in addition to 4-acetyl-propylbenzoate, to the formation of 4-chloro-propylbenzoate in 20 % yield, 1,4-benzenedioic acid propyl ester (dipropyl terephthalate) in 19 % yield, 4-propoxy-acetophenone in 1.6 % yield and 4-propoxy-propylbenzoate in 1.1 % yield (*Figure 3- 9*).

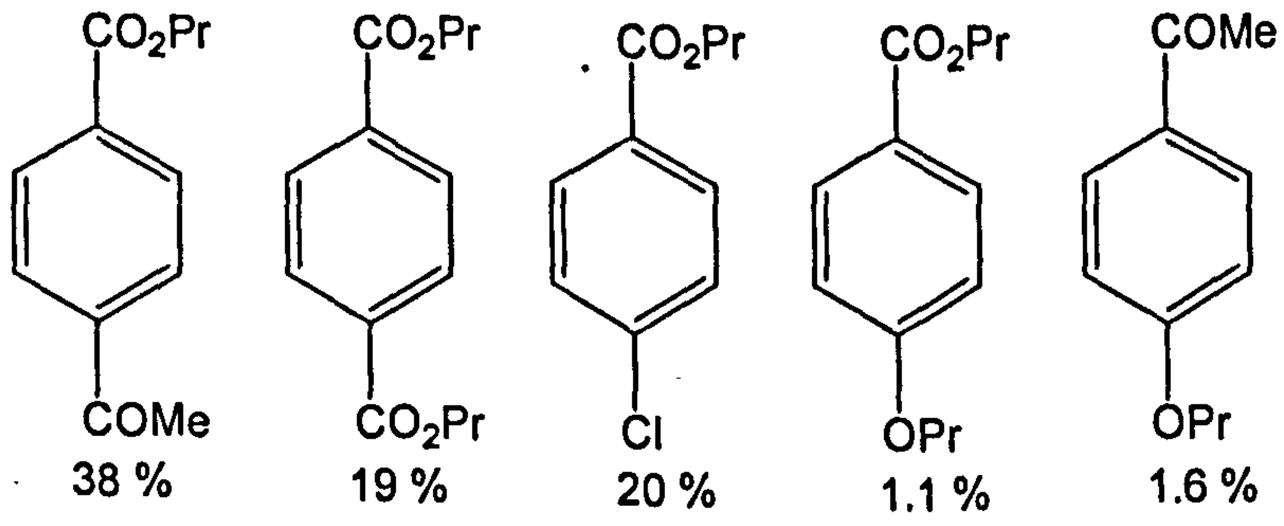


Figure 3- 9: Structure of 1, 4- propyl benzodiate, 4-chloro-propylbenzoate, 4-propoxy-propylbenzoate and 4-propoxy-acetophenone

The starting material may undergo either nucleophilic attack of the alcohol to the carbon atom carrying the chlorine atom to yield 4-alkoxyacetophenone or addition to the palladium complex to form the active species in the catalytic

cycle, which will insert CO to form the palladium-acyl intermediate leading eventually to the 4-acetyl-alkylbenzoate (*Figure 3- 10*). If the nucleophilic attack of the alcohol upon 4-chloroacetophenone is fast compared with the coordination to the metal centre and CO insertion, the yield of 4-alkoxyacetophenone and 4-alkoxy-alkylbenzoate will be higher than that of 4-acetyl-alkylbenzoate. In methanol the former reaction is apparently fast compared with the latter, since no 4-acetyl-methylbenzoate was produced.

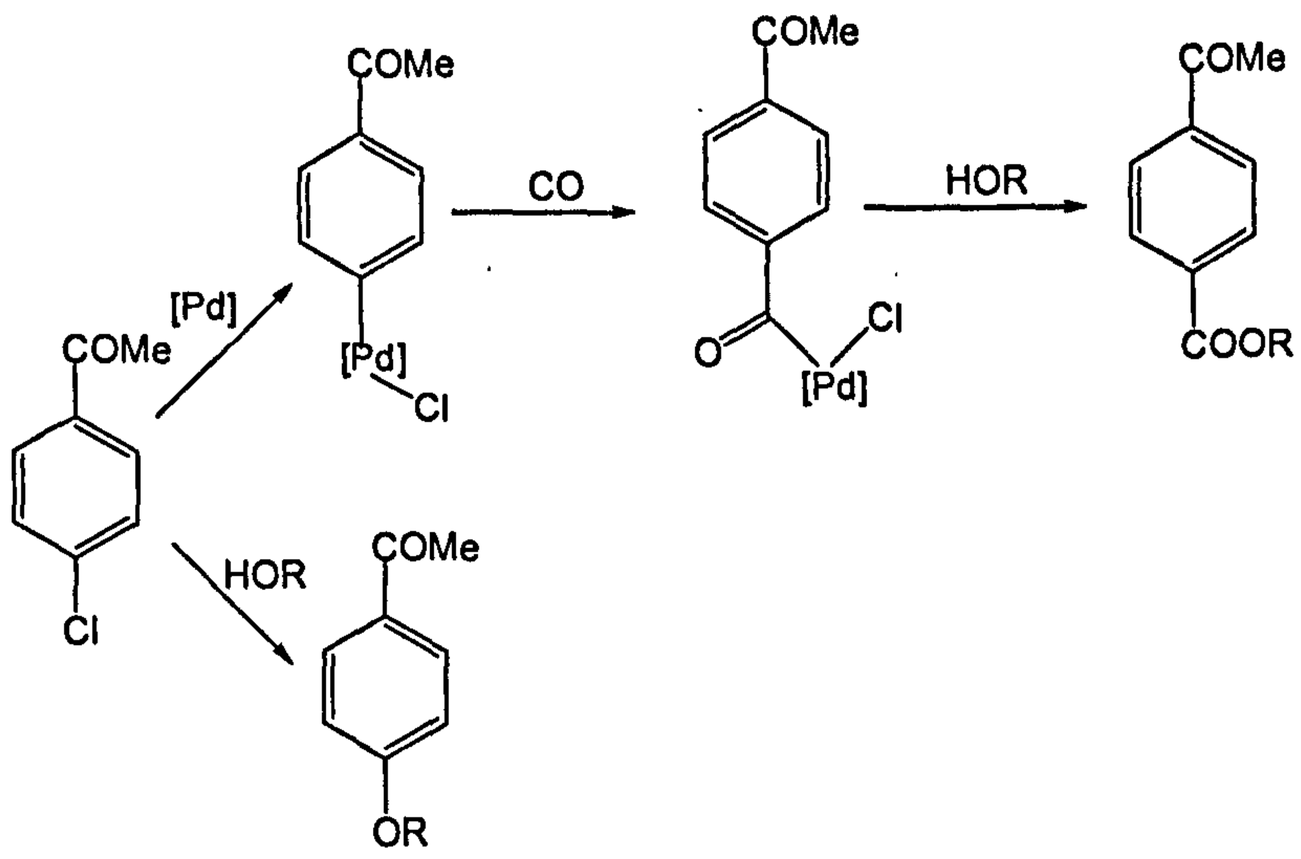


Figure 3- 10: Nucleophilic aromatic substitution vs carbonylation

3.2.2.5. Labelling studies.

These studies involved the use of CD_3OD, CD_3OH and ^{13}CO and show that dimethyl terephthalate is not formed by direct methoxycarbonylation of 4-chloro-acetophenone but by a two step reaction *via* 4-chloromethylbenzoate.

3.2.2.5.1. CD_3OH as solvent.

The use of d^3-methanol confirmed that the methoxy groups present in methyl benzoate, 4-chloro-methylbenzoate and dimethyl terephthalate come from the nucleophilic attack of methanol.

The labelling results are shown in Table 3- 6. These results showed that no H/ D exchange took place either in the ring or in the methyl group of the acetophenone (*Figure 3- 11*).

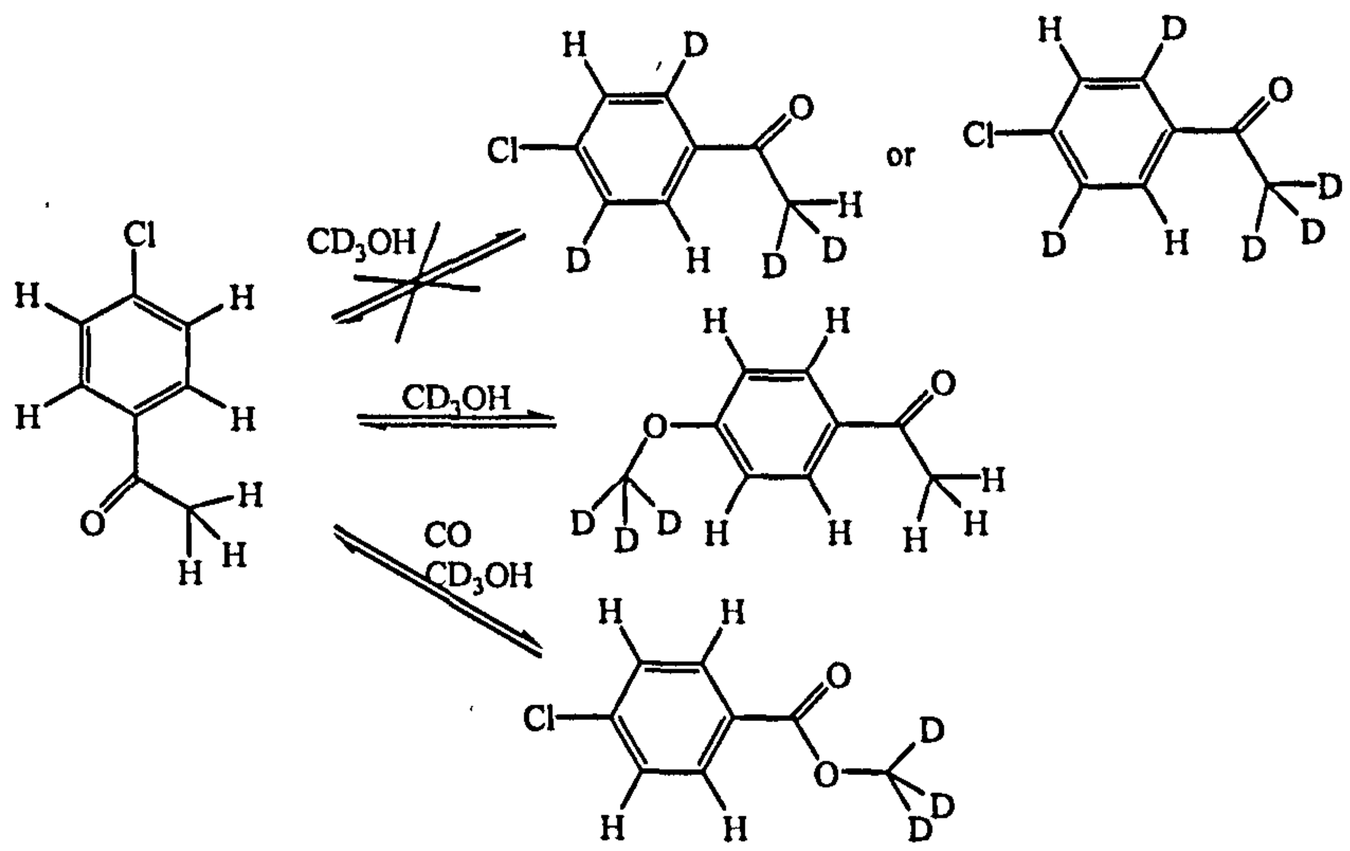
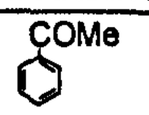
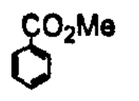
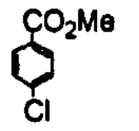
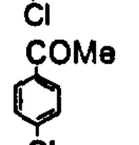
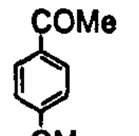
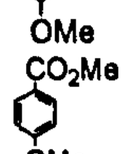
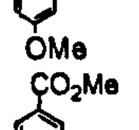


Figure 3- 11: Products observed when using CD_3OH.

Table 3- 6: Deuterium atoms in each product

Substrate	d^0	d^1	d^2	d^3	d^4	d^5	d^6	d^7
	0	0	0	0	0	0	0	0
	0	0	0	100	0	0	0	0
	0	0	0	100	0	0	0	0
	0	0	0	0	0	0	0	0
	0	0	0	100	0	0	0	0
	0	0	0	0	0	0	100	0
	0	0	0	0	0	0	100	0

The unreacted 4-chloroacetophenone remains unaffected by the presence of CD_3OH, since neither the protons of the ring nor the protons of the methyl group exchange with the deuterium from the methanol. However, 4-chloroacetophenone (R= -COMe) undergoes either nucleophilic aromatic substitution of the chlorine by a methoxy group or via a benzyne intermediate (see section 3.2.2.5.2). The same possible mechanisms can be applied to the formation of 4-methoxy-methylbenzoate (R=-COOMe). This methoxy group comes from the d^3-methanol and therefore 4-methoxy-acetophenone contains three deuterium atoms and 4-methoxy-methylbenzoate contains six (Table 3- 6). The important observation is that the ester group in 4-chloro-methylbenzoate contains 3 deuterium atoms so that it formally arises from nucleophilic displacement of CH_3^- by $^-OCH_3$. This is discussed in section 3.2.2.5.3.

3.2.2.5.2. CD_3OD as solvent.

Further evidence concerning the origin of 4-methoxyacetophenone and 4-methoxymethylbenzoate is provided by reactions carried out in CD_3OD (Table 3- 7 and *Figure 3- 12)*. Incorporation of D into the ring *ortho-* to the methoxy group would indicate the participation of benzyne. A benzyne intermediate is formed by elimination of two mutually *ortho-* groups, chlorine and hydrogen in this case, to form a triple bond as part of the aromatic ring. Because of the rigid geometry of the ring and the unfavourable angles of the overlapping orbitals, this new bond is very weak making benzyne a highly reactive intermediate. Benzyne undergoes rapid nucleophilic addition of CD_3O^- to yield a carbanion which then takes a D^+ from the reaction medium to yield 4-methoxyacetophenone containing a deuterium atom in the aromatic ring (*Figure 3- 13*).

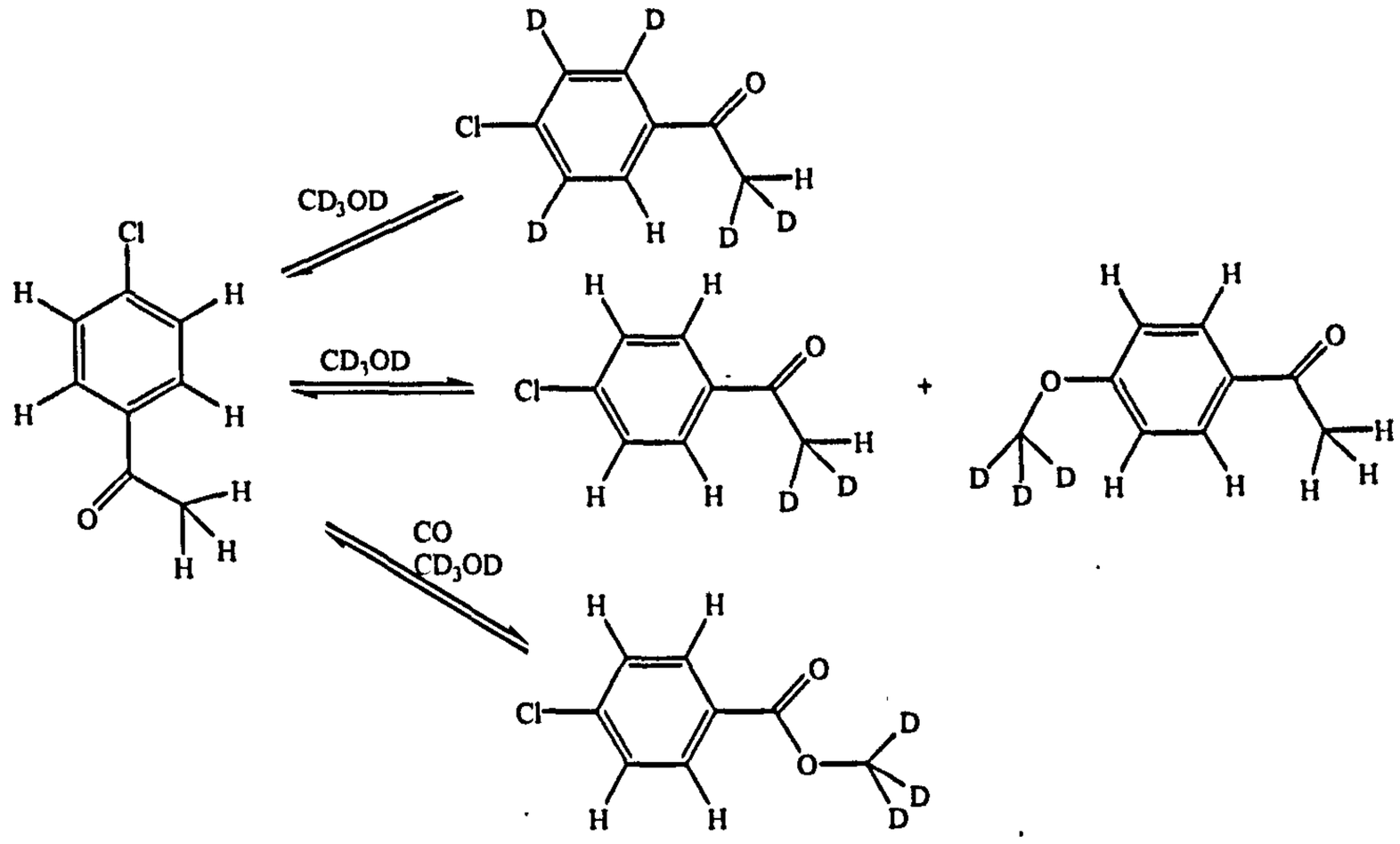


Figure 3- 12: Products observed when using CD_3OD.

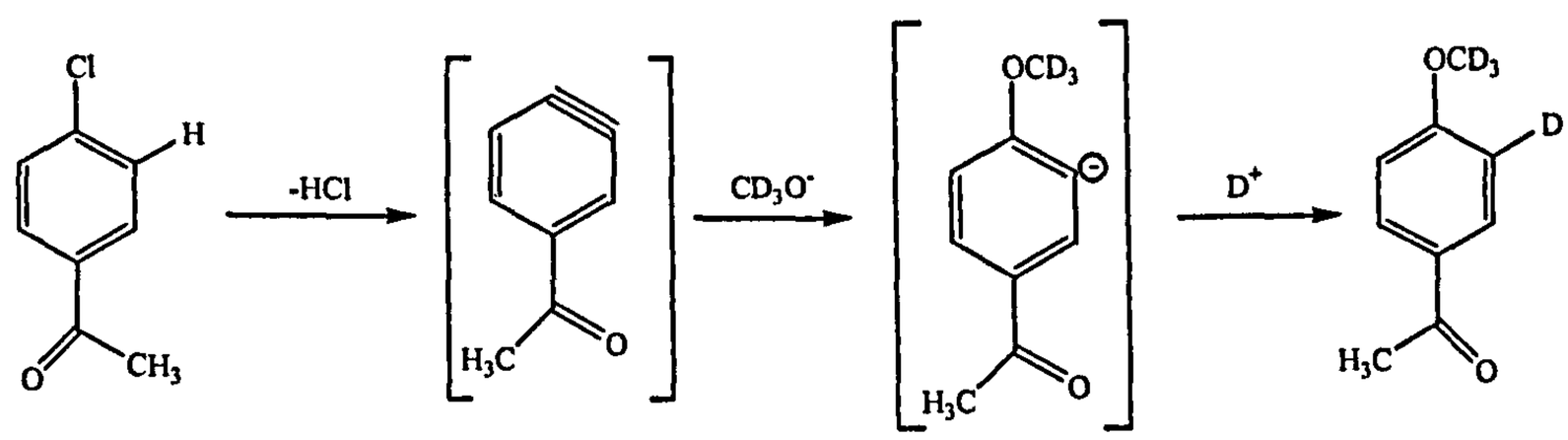
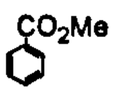
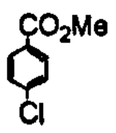
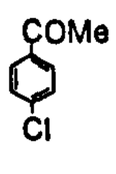
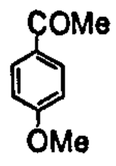
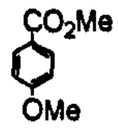
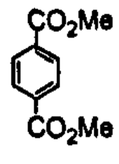


Figure 3- 13: Formation of 4-methoxyacetophenone via benzyne mechanism

The unreacted 4-chloroacetophenone contains 1-6 D atoms (predominantly 2-5). Up to 3 D atoms can be explained by keto enol tautomerism and exchange of the enol H with D from the solvent. The other two D atoms must reside on the ring. A possible mechanism for their incorporation involving activation of an *ortho*-C-H bond of an O bound substrate molecule is shown in *Figure 3- 14*. The small amount of incorporation of a 6th D atom suggests that more general H/D exchange into the ring is also possible. The predominance of d^4-acetophenone suggests that it contains 3 D atoms on the methyl group (keto-enol exchange with the solvent) and a D atom in the 4 position. This must come from the OD group of the solvent since it is H when CD_3OH is used. The comparative lack of

acetophenone containing > 4 D atoms suggests that it forms early in the reaction and does not itself undergo *ortho-* C-H/D exchange. 4-methoxyacetophenone contains 4-7 D atoms (predominantly 6) showing that little ring deuteriation has occurred and especially that it is formed by nucleophilic substitution of the chloride rather than by a benzyne mechanism which would be expected to give much more d^7 product. Again, *ortho-* C- H/D exchange does not seem to occur readily in this case and is not very prevalent in the compounds derived from 4-chloromethylbenzoate.

Table 3- 7: Deuterium labelling with d^4-methanol.

Substrate	d^0	d^1	d^2	d^3	d^4	d^5	d^6	d^7	d^8
	0	0	7.5	31.8	55.5	5.2	0	0	0
	0	0	0	16	69	11	4	0	0
	0	0	3.4	62.3	10.1	20.9	3.3	0	0
	0	3.1	20.1	47	12.5	15.3	2	0	0
	0	0	0	0	4.4	28	60.4	7.2	0
	0	0	0	0	0	4	86.7	9.3	0
	0	0	0	0	0	0.7	84.1	13.8	1.4

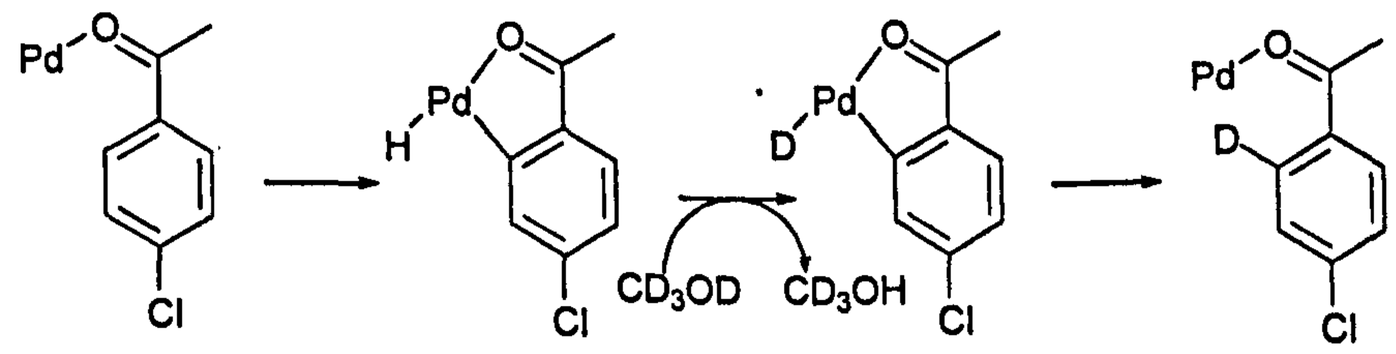


Figure 3- 14: Proposed mechanism for the incorporation of a deuterium in ortho- relative to the aceto group

3.2.2.5.3. ^{13}CO as carbon monoxide source.

Reactions performed with ^{13}CO in MeOH and *n*-PrOH confirm that only one of the two acetyl groups of either dimethyl terephthalate or 1,4-propylbenzodiate contains ^{13}C, i. e. is formed by palladium catalysed methoxycarbonylation and hence the carbonyl group in the ester derived from the ketone is that which was originally in the 4-chloro-acetophenone (*Figure 3- 15*). This is further confirmed by the lack of ^{13}C in 4-chloromethylbenzoate, whose methoxy group comes from the solvent as previously noted. Thus, nucleophilic substitution of the methyl group of the 4-chloroacetophenone by a methoxy group must occur, implying that a methyl group would be forced to act as a leaving group.

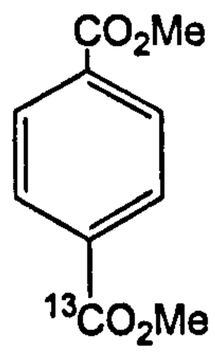


Figure 3- 15: Dimethyl terephthalate containing ^{13}CO

In order to simplify the problem an experiment in n-propanol (a more selective nucleophile) with labelled carbon monoxide was carried out. Doing so, it was possible to confirm that only one of the two ester groups present in the dipropyl terephthalate is produced catalytically. The products and yields obtained were the same as those obtained with non labelled carbon monoxide. Interestingly, 4-chloro-propylbenzoate had a non labelled carbon atom in the ester group, confirming that the organic reaction taking place is the substitution of the methyl group of the acetophenone by a propoxy group coming from the alcohol. To understand completely the mechanism of the reaction, it was necessary to find out the form in which the methyl group is eliminated, since it is well known that

methyl groups are bad leaving groups due to the instability of the possible anion $^{-}CH_3$. Some possibilities were considered: methane, acetaldehyde or as a part of an alcohol which has one carbon atom more than the original. Careful GC analysis of all the products obtained, both in the liquid and gas phases shows that ^{13}C only appears in the terephthalates and in methyl or propyl formate. The formates are also formed in the absence of substrate, so they are probably not relevant to the transformation of the ketone into an ester. Unfortunately, we have not been able to identify the fate of the methyl group which "leaves" the ketone and the mechanism operating in this reaction remains unsolved. Nevertheless, a similar kind of C-C bond cleavage of aryl methyl ketones to produce aryl carboxylic acids under mild conditions has been recently reported by Vozzolo[13]. In this work they claim that by treatment of a highly electron deficient aryl methyl ketone with DMF·DMA in methanol under reflux for 16 hours yielded the desired ester in >50 %, being 95 % for 1-(4-nitro-phenyl)-propan-1-one. The mechanism proposed for the formation of aryl methyl esters in this manner requires the transformation of DMA into an enamine, which will be hydrolysed to yield an aldehyde. A previous report by Petric[14] showed that after treating aryl methyl ketones with an excess of KOH in DMF at 65-68 °C, the desired carboxylic acid was produced in more than 80 % yield. No mechanism was proposed in this paper, although this method was supposed to be complementary to methods of oxidative cleavage of ketones, like haloform reaction, Baeyer-Villiger oxidation and an extension of the Haller-Bauer reaction.

3.3. Conclusions

Selective carbonylation of aromatic chlorides to carboxylic acid esters is catalysed by Pd/DTBPMB complexes in alcohols in the presence of base, provided that the aromatic ring is very electron poor. For less activated aromatic rings such as that in 4-chloroacetophenone, selective carbonylation can only be achieved by using alcohols of low nucleophilicity, such as 2,2,2-trifluoroethanol. More nucleophilic alcohols give many side products arising from nucleophilic aromatic substitution, H for Cl exchange and an unusual transformation of the methylketone into a methyl ester. Labelling studies show that this reaction formally occurs by displacement of the methyl group by methoxide. Nitro and cyano groups on the ring also undergo severe side reactions.

3.4. References.

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18. Bayer A., Canty A.J. and Edwards P.G., *J.Chem. Soc. Dalton Trans.*, **19** (2000), 3325

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27. Grate J., Hamm D., Valentine D., US4629804, 1986

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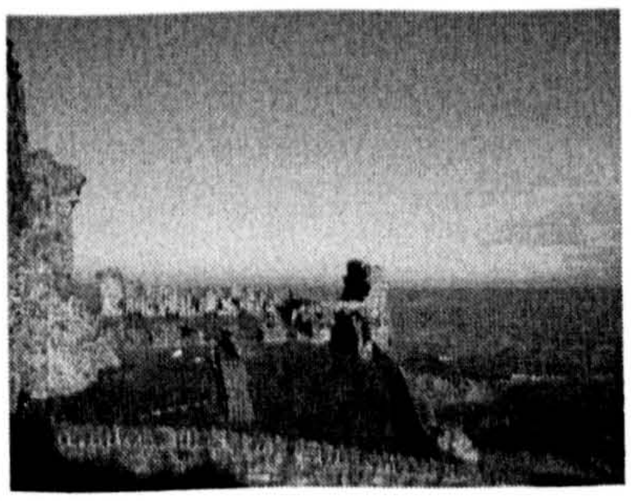
Chapter 4:

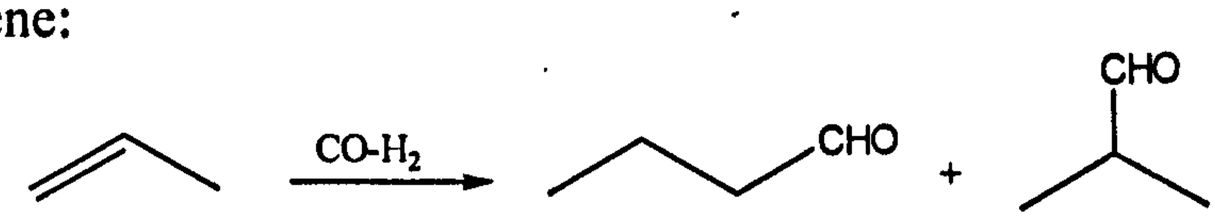
HYDROFORMYLATION OF ALKENES



4.1. Hydroformylation of alkenes

One of the most important homogeneous catalytic reactions is hydroformylation, which consists of the addition of CO and H_2 to an alkene to produce aldehydes. Two different products can be obtained from this reaction. The linear aldehyde is formed by carbonylation of the terminal carbon atom whereas the branched is formed by carbonylation of the internal carbon atom of the double bond. The interest is usually in obtaining the linear aldehyde. Therefore, research is focused on maximising the production of this product over the branched.

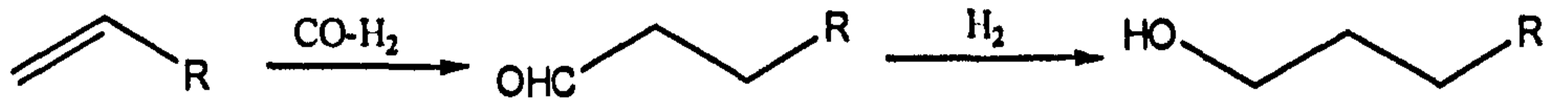
The most typical example of a hydroformylation reaction is the production of butanal from propene:



Scheme 4- 1: Hydroformylation of propene

Aldehydes are a very versatile group of chemicals since they can be used as starting materials for the production of many other compounds. For instance, butanal is produced on a scale of four million tons per year and it can be hydrogenated to form 1-butanol, which is extensively used as solvent, or it can condense to form 2-ethylhexanol, which is then converted to esters for use as plasticizers.

Long chain alkenes can also be hydroformylated in order to produce fatty alcohols, which are starting materials in the synthesis of biodegradable detergents and plasticizers. The production of alcohols in one single step from an alkene and synthesis gas requires the presence of a catalytic system effective for both hydroformylation and hydrogenation.



Scheme 4- 2: Indirect formation of alcohols from hydroformylation of alkenes

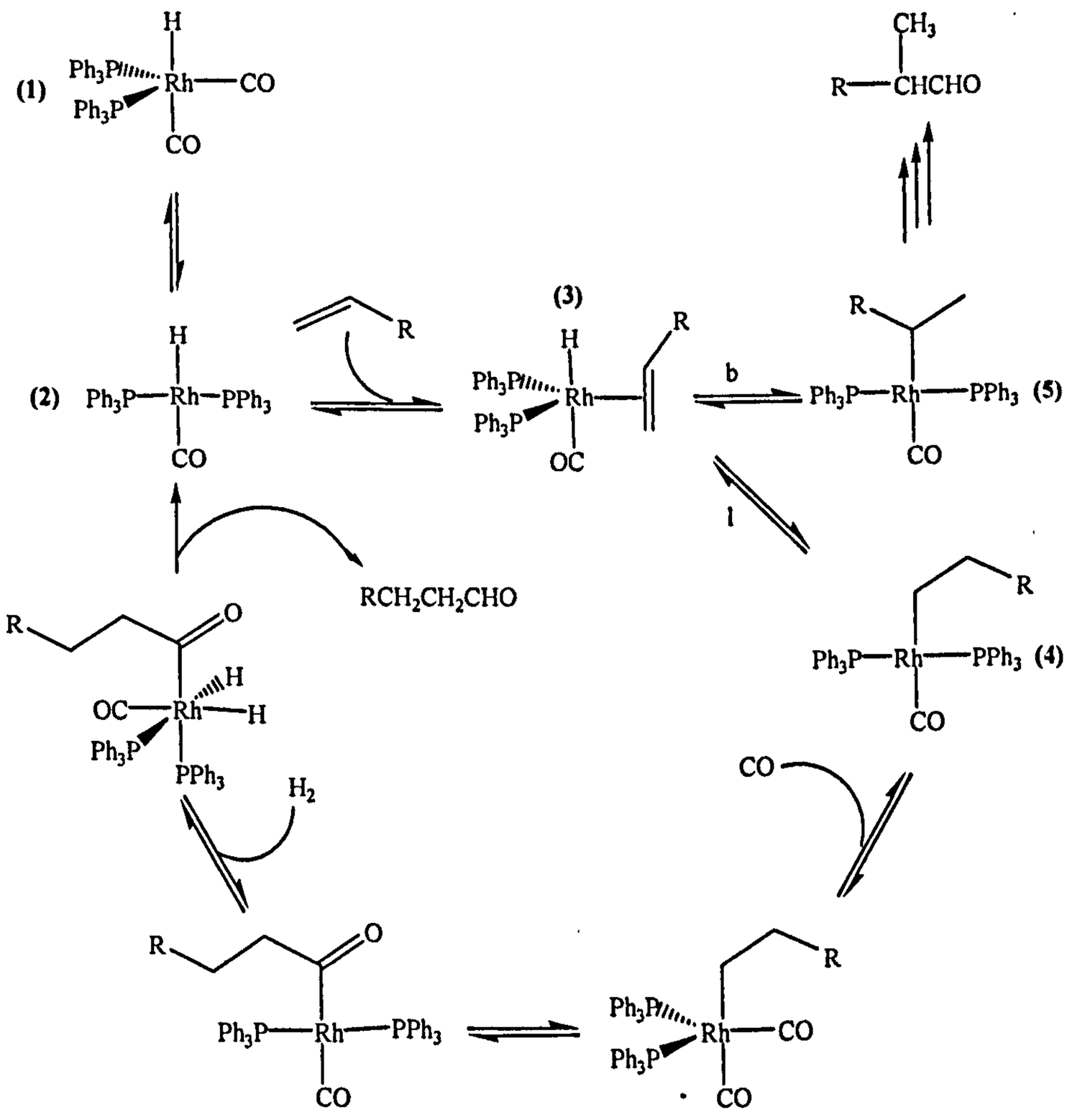
Catalysts based on cobalt carbonyl without phosphine ligands $Co_2(CO)_8$ were the first ones commercialised. This compound generates $HCo(CO)_4$ as the active species in the mechanism proposed by Heck and Breslow.[7]

This process requires very harsh conditions (120°C-140°C and 200 bar of $CO-H_2$) due to the low reactivity of the cobalt complexes. On the other hand, yields from 70% to 90% to aldehydes are reached even when internal alkenes are starting materials. Although this kind of catalyst is reasonably good for industrial processes, their use implies several problems during product purification and catalyst recycle steps.

Phosphine-modified cobalt carbonyl catalysts yield linear alcohols very selectively in one step, since they are also very active hydrogenation catalysts. In 1966 Shell reported[1] a process in which, by using trialkyl phosphine and cobalt carbonyl, it was possible to combine hydroformylation and hydrogenation steps satisfactorily. In spite of being less active than unmodified cobalt carbonyl catalysts for hydroformylation, they were much more active for hydrogenation (~10 % of the alkene was hydrogenated to alkane), giving l: b ratios of 7:1 to linear alcohols instead of 4:1 given by cobalt carbonyl. In addition, lower pressures were required, facilitating the engineering of the reactor.

Rhodium catalysts can hydroformylate alkenes under milder conditions. Initially there was no interest in them because branched aldehydes were formed rather than linear.

It was in the mid-sixties when Wilkinson[2, 3] and co-workers discovered a process in which, by using arylphosphines to modify the rhodium precursor, very active catalysts were obtained. In addition excellent selectivities towards the linear aldehyde were achieved. The mechanism proposed to operate is shown in *Scheme 4- 3*. In 1976 Union Carbide Corporation commercialised the first phosphine-modified rhodium catalyst. This catalyst was based on triphenylphosphine and it is the well known $[Rh(H)(PPh_3)_3(CO)]$.



Scheme 4- 3: Rhodium-catalysed hydroformylation mechanism

However, not everything favours the use of rhodium catalysts, since the high cost of the metal and its recycling are still a problem. By using a heterogeneous catalyst the recycling would not be a problem anymore, but selectivity towards the linear products might decrease. Another way to overcome this problem could be

the use of biphasic systems, which can consist of water+organic liquid, non-polar organic liquid+polar organic liquid, ionic liquid+organic liquid or fluorous organic phase+organic liquid.

The Ruhrchemie-RhônePoulenc process[29] is an example of the extremely successful results achieved using liquid biphasic systems. This process was commercialised by Celanese in 1984 for hydroformylation of propene.[26] In 1995 an additional plant to produce pentanal from butene was erected. The catalyst used is a rhodium complex of sodium tri-(m-sulphonyl)triphenylphosphine (tppts) which is soluble in water.[26] Under the reaction conditions these two phases mix so that the substrate contacts the water soluble catalyst and when the system is cooled, the aldehydes will be in the organic layer whereas the catalyst will remain in the aqueous layer. The hydroformylation of long chain alkenes does not occur at a reasonable rate, since they are insufficiently soluble in water.

Simultaneously to the development of triphenylphosphine, phosphites became very popular, however it is only recently that scientists have commecialised them by making stable bulky monophosphites[4a,b, c,5] and diphosphites.[6]

Diphosphines have been used in catalysis since the late fifties. It was not until the mid-sixties when Iwamoto and Yuguchi reported advantageous results using iron catalysts modified with several diphosphines of different bridge length.[27]

4.1.1. Diphosphines

The effect of bidentate phosphines as ligands in hydroformylation reactions has aroused considerable interest since their use greatly improves the l: b ratios relative to those obtained when monophosphines are used. The first use of a diphosphine ligand, such as diphenylphosphinoethane (dppe), hydroformylation

was published in1962 by Heck and Breslow.[8] They reported that unknown complexes where formed from the reaction of dppe and $Co_2(CO)_8$.

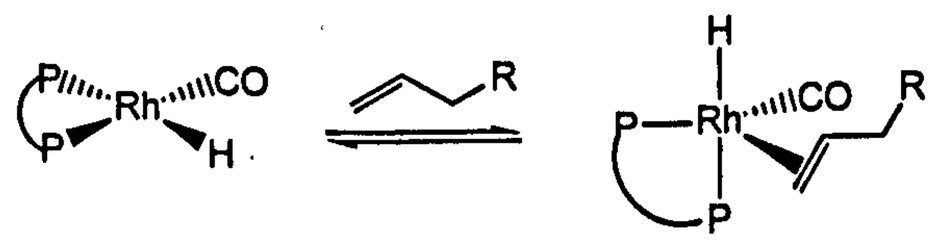
Only a few years later Slaugh and co-workers reported the use of the cobalt carbonyl modified by dppe for catalysed hydroformylation.[9] This report proved that this system gave worse rates and selectivities than when PBu_3 modified cobalt catalysts or non-modified cobalt carbonyl were used.

Pittman studied the hydroformylation of 1-pentene when diphosphine ligands like dppe, dppp or dppb were added to $Rh(H)(CO)(PPh_3)_3$.[10] In all cases he found low values of l:b ratio. This observation can be explained in two ways: (1) the cis-chelating diphosphines in the presence of the rhodium precursor form the complex A, which is in equilibrium with complex B (*Scheme 4- 4*), which in turn is known to be less selective.[24]

Complex A Complex B

Scheme 4- 4: Pentacoordinated and tetracoordinated rhodium species in equilibrium

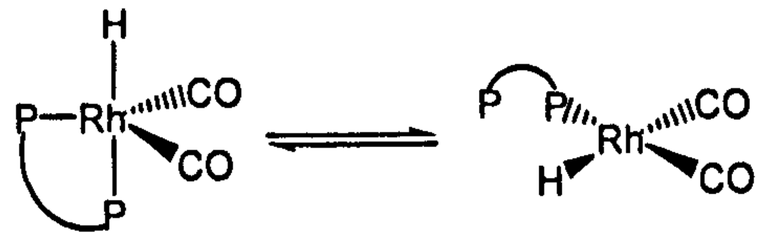
Alternatively, species B can coordinate an alkene to give complex C, in which the diphosphine occupies apical-equatorial orientation (*Scheme 4- 5*). Again this is known to give low selectivities compared with the isomer containing both phosphorus atoms in equatorial position.[24]



Complex B Complex C

Scheme 4- 5: Coordination of the alkene

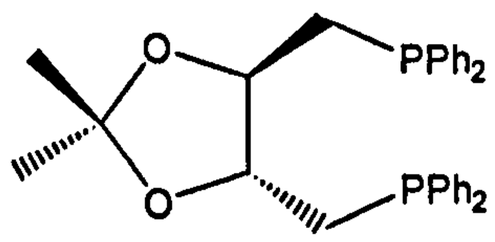
There is also another possible way of explaining the lower selectivity. Complex A is able to undergo dissociation of one phosphine to give species D (*Scheme 4- 6*), in which only one phosphorus atom is bound to the rhodium atom and this also leads to low selectivities.



Complex A Complex D

Scheme 4- 6: Dissociation of one phosphorus atom.

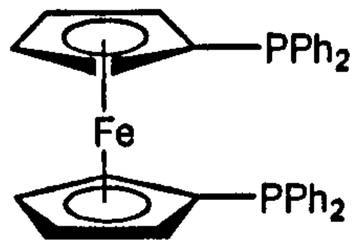
Consiglio and coworkers first reported the use of [Rh(H)(CO)(PPh_3)$_3$] modified with DIOP in 1973 aiming at asymmetric hydroformylation of alkenes (*Scheme 4- 7*). They reported l: b ratios of around 13: 1 under mild conditions.[11] Previous work reported by Wilkinson[12] using Rh(H)(CO)(PPh_3)$_3$ in the presence of a large excess of PPh_3 showed l:b ratios of 20: 1 when the reactions were carried out at 80°C under 7 bar of CO-H_2. Further work by Van Leeuwen and co-workers using [Rh(cod)(OAc)$_2$] and TPP to hydroformylate 1-pentene[13] or using [Rh(CO)$_2$(dipivaloylmethanoate] and TPP for 1-octene hydroformylation[14] showed l: b ratios not higher than 3.6: 1. Hence, the use of DIOP in rhodium hydroformylation of alkenes was the first example of improvement of l: b ratios by using bidentate ligands.



Scheme 4- 7: Structure of DIOP

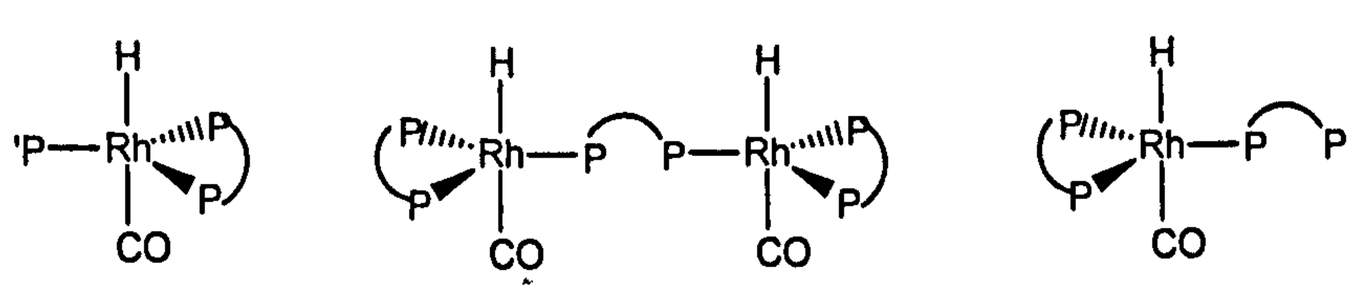
Ferrocene diphosphine ligands based on 1,1'-bis(diphenylphosphino)ferrocene (dppf) (*Scheme 4- 8*) modifying rhodium catalysts were first reported by Unruh and

Christenson in 1982.[15] The P-Rh-P angle formed varies between 92°-120°, preferring 97°± 2°. Also the two cyclopentadienyl groups can turn, which confers flexibility to the ligand, so it can accommodate a variety of bridging structures.



Scheme 4- 8: Structure of dppf

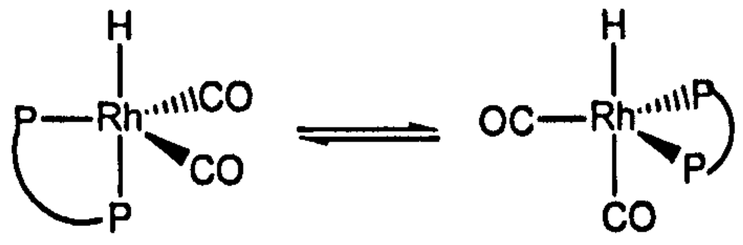
Unruh and co-workers also studied the effect of P: Rh ratio on the selectivity towards the linear aldehyde. They carried out the hydroformylation of 1-hexene at 140°C and 7.9 bar of synthesis gas changing the ligand: Rh ratio from 1 to 3. The highest selectivity towards heptanal, 83 %, was obtained when ligand: Rh = 1.5. No further improvement was reached by increasing the ligand: Rh ratio. Consequently, not only did they conclude that there were 3 species in equilibrium, but also that the dimeric species shown in *Scheme 4- 9* was the most selective one.



Scheme 4- 9: Rhodium species in equilibrium

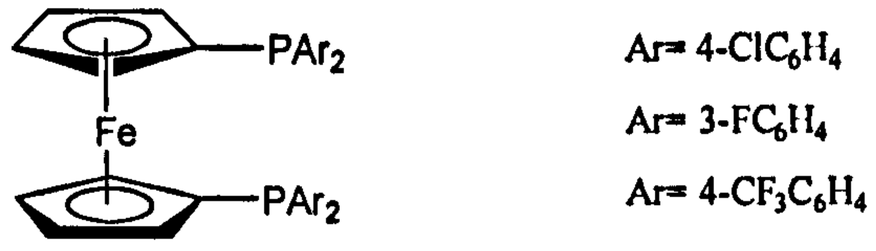
The existence of all these intermediates has been proven by ^{31}P NMR studies[16]. These NMR experiments were carried out at higher catalyst concentration and with no CO added, whereas in the catalysis experiments the concentration of free ligand was at most 1.2 mM ([Rh]= 0.6 mM) and the pressure of CO was 4 bar.

Van Leeuwen and co-workers have recently shown that the dppf-Rh system behaves differently under synthesis gas. Their NMR and IR studies have confirmed the presence of only two species in rapid equilibrium (*Scheme 4- 10*).



Scheme 4- 10: Apical-equatorial and bisequatorial rhodium species

Unruh and co-workers also studied modified dppf ligands. The modification consisted of substituting the phenyl groups with electron withdrawing groups (*Scheme 4- 11*).

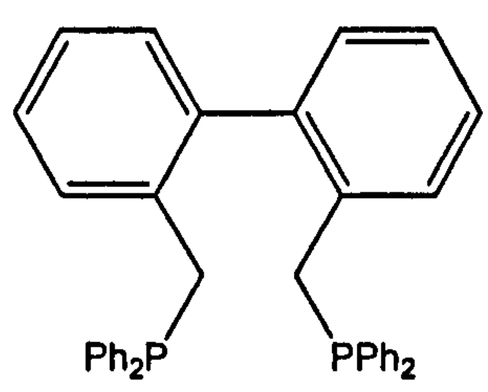


Scheme 4- 11: Modified dppf

This allowed a study of the effect of the ligand basicity on the l: b ratio. By increasing the electron withdrawing capacity of the phenyl groups, the basicity of the ligand decreases. As a result, an increase in the rate and the l: b ratio takes place. Other reasons for changes in l:b ratio are discussed in section 4.1.2. The increase in the rate can be understood in the basis of an easier dissociation of CO due to a lower π-back donation from the metal to the CO. The higher selectivity to linear aldehyde shows that the terminal alkyl intermediate is intrinsically favoured when the basicity of the ligand decreases. β-hydride elimination in the rhodium-alkyl species forms the branched alkyl rhodium intermediate, which can either reform 1-hexene or form 2-hexene. The selectivity to the linear aldehyde decreases whilst the amount of internal alkenes increases.

In 1987 Devon and coworkers reported very high selectivity to linear aldehyde when a new diphosphine, BISBI (*Scheme 4- 12*), was used for the hydroformaylation of propene (l:b= 30). The use of 1-hexene as the substrate led to a l:b ratio of 66.[22] The measured bite angle of BISBI turned out to be 112°, much greater than that of all the ligands commonly used.[23] A mechanistic study

carried out by Casey[23] showed for the first time the coordination of a diphosphine in a bisequatorial fashion rather than apical-equatorial coordination mode. The l:b ratios afforded until then were lower than those obtained with BISBI. Thus, the high regioselectivity observed could be related to the bis-equatorial coordination or to the wider bite angle increasing the steric congestion around the metal and therefore destabilizing the branched alkyl intermediate.

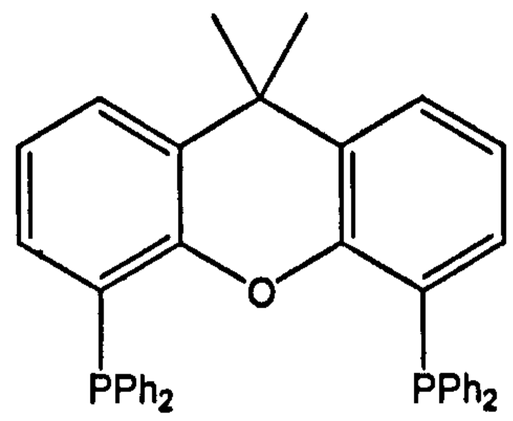


Scheme 4- 12: Structure of BISBI

Unfortunately, steric arguments failed to explain the high regioselectivity observed for diequatorial chelates.[24] Therefore, electronic difference between bis-equatorial coordination and apical-equatorial coordination must be considered. Having two strong σ-donor phosphorus atoms in the equatorial plane, strong π-back donation from the rhodium to the coordinated alkene in the equatorial plane would be expected, favouring the insertion of the alkene into the Rh-H bond to form the 1-alkyl-rhodium intermediate which leads to the linear aldehyde.

A new family of ligands derived from Xantphos (*Scheme 4- 13*) having a variety of bite angles from 102° to 121° were synthesised and tested for the hydroformylation of 1-octene.[24,25] A correlation between the increase on the bite angle from 102° to 111° and the increase on the rate and the l:b ratio was reported. However, wider bite angles do not give greater enhancement. An increase of the accepting ability of the phosphine also leads to high rates and l:b ratios. By lowering the basicity of the phosphine not only does the preference for the bis-equatorial coordination mode increase, explaining the high l:b ratios observed,

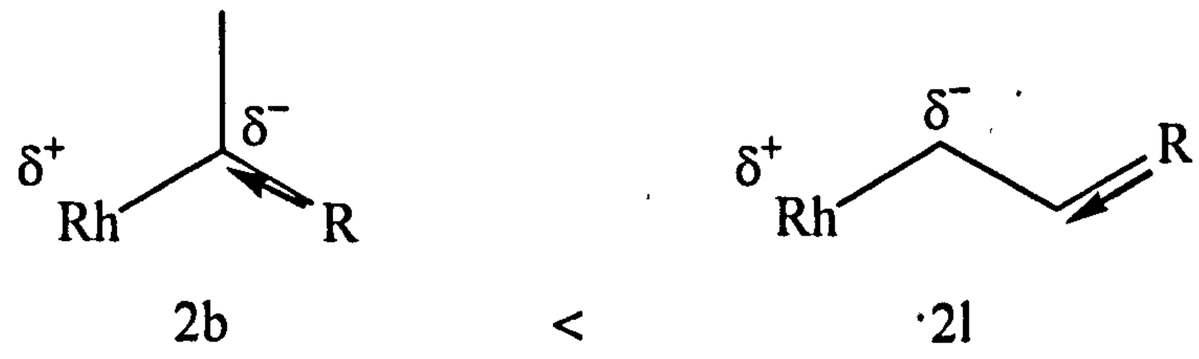
but also facile dissociation of CO and alkene coordination are allowed, explaining the high rates.



Scheme 4- 13: Structure of Xantphos

4.1.2. Regioselectivity

The increasing l:b ratio with widening the bite angle for DIOP (85°)/ dppe (102°)/ Xantphos (111°)/ BISBI (113°) is associated with the greater preference for the bisequatorial coordination in all species involved in the selective formation of the linear aldehyde. The H migration onto the alkene to form Rh-alkyl is fast and reversible via β-hydrogen abstraction. Both the linear and branched Rh-alkyl intermediate have a similar structure, the linear being slightly favoured on steric and electronic grounds (*Scheme 4- 14*). Hence, they are formed in similar amounts and so are the corresponding aldehydes.



Scheme 4- 14: Formation of the linear and branched Rh-alkyl intermediates

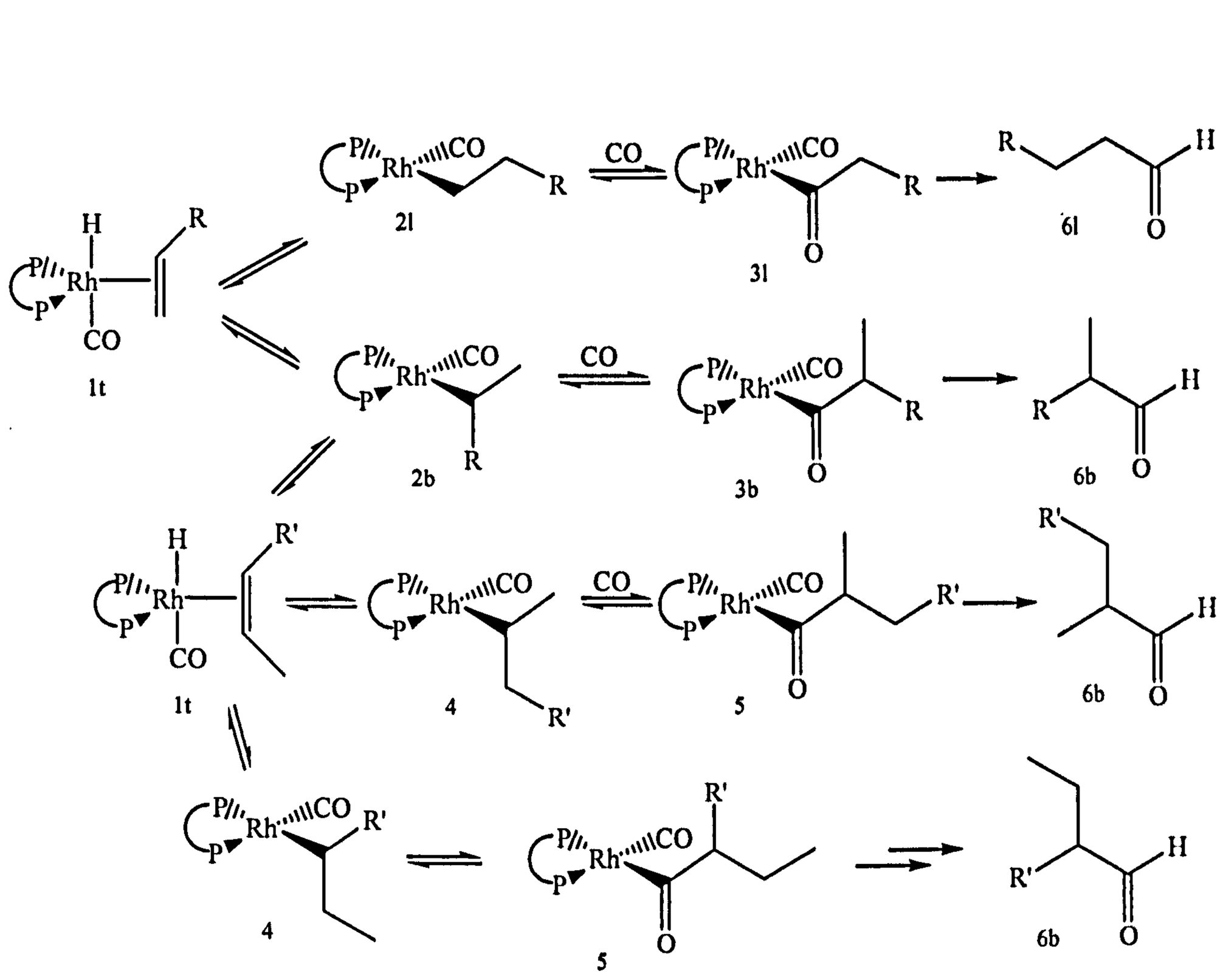
If the linear and branched Rh-alkyl intermediates are in equilibrium, the regioselectivity is determined by the relative rates of H migration and CO addition. A low linear selectivity may be caused by (*Scheme 4- 15*):

a) Low selectivity in the formation of **2l** and fast CO addition to trap any Rh-alkyl formed leading to **3l** and **3b**. If the steric congestion caused by the

ligand around the metal is not large, the difference in the steric interaction of the two Rh-alkyl intermediate **2l** and **2b** will be small and the former will be slightly favoured for electronic reasons. Therefore, the Rh-acyl intermediates **3l** and **3b** will be formed in similar amounts leading to low l:b ratios. Here the branched isomer will predominantly be 2-methyl-hexanal (1-hexene as the substrate).

b) Fast isomerisation followed by hydroformylation. Fast β-hydrogen abstraction in **2b** leads to the formation of rhodium species containing internal alkenes, **1i.** The internal alkene may decoordinate and the l:b ratio will be determined by whether or not the internal alkenes hydroformylate. If they do not, the reaction will be characterised by a low selectivity to aldehydes and high l:b ratio (most of the branched alkyl leads to isomerised alkene rather than branched aldehyde). If the internal alkenes do hydroformylate, the l:b ratio will be low and there will be significant amounts of 2-ethyl-pentanal (1-hexene as the substrate).

c) Slow CO addition to **2l.** The linear Rh-alkyl intermediate **2l** is slightly favoured thermodynamically over **2b** and highly favoured kinetically. However, if **2l** is not efficiently trapped by CO, equilibrium is established between **2l** and **2b** via β-hydrogen abstraction thus increasing the amount of **2b** formed to the thermodynamic proportion.



Scheme 4- 15: Regioselectivity control

In this chapter a detailed study of hydroformylation of different alkenes will be presented. Different parameters, such as rhodium precursors, ligands, solvents, pressure or temperature among others will be analysed and discussed. In addition, a study of the mechanism will be carried out, placing special emphasis on the chloro containing intermediates.

4.2. Hydroformaylation of alkenes.

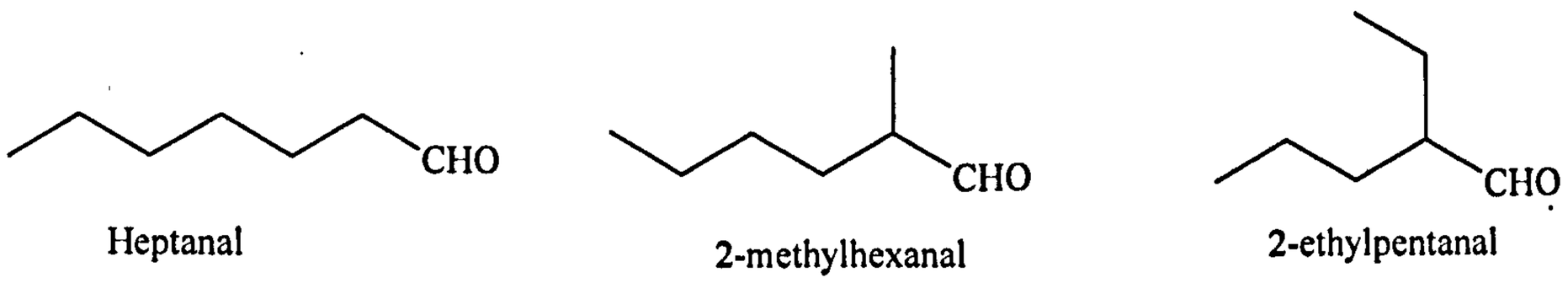
One of the main targets of this project was the successful hydroformylation of alkenes. After the successful production of esters by the methoxycarbonylation of alkenes, we turned our attention to the preparation of aldehydes by reaction of an alkene with CO: H_2.

In order to evaluate the effectiveness of DTBPMB, hydroformylation of 1-hexene, 1-octene and allyl alcohol was carried out using different rhodium precursors and several solvents.

4.2.1. Hydroformylation of 1-hexene.

The hydroformylation of 1-hexene was carried out using $[RhCl(CO)_2]_2$, $[Rh_2(OAc)_4]$, $[RhCl_3 \cdot H_2O]$ and $[Rh(acac)(CO)_2]$ as rhodium precursors.

The expected products from this reaction are heptanal and 2-methylhexanal, although 2-ethylpentanal (*Figure 4- 1*) can be formed since isomerised hexenes might also be hydroformylated.



Heptanal | 2-methylhexanal | 2-ethylpentanal

Figure 4- 1: Expected products from the hydroformylation of 1-hexene.

4.2.1.1. $[RhCl(CO)_2]_2$ as catalytic precursor.

Using $[RhCl(CO)_2]_2$-DTBPMB complexes as the catalytic system, different parameters, such as solvent, pressure, ligand and CO/H_2 ratio have been studied in detail. The results obtained are discussed in the following sections.

4.2.1.1.1. Effect of different solvents.

Three different solvents were tested: toluene, THF and OctMiMTfN (as an ionic liquid). In the three cases high conversion was observed and especially for toluene or OctMIMTfN reasonable selectivity towards heptanal (Table 4- 1 and *Figure 4- 2*).

Table 4- 1: Hydroformylation of 1-hexene with $[RhCl(CO)_2]_2$-DTBPMB.

[Rh] (M)	[L] (M)	Solvent	Conv (%)	S ald (%)	S linear (%)
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	100	100	74.9
$3.83x10^{-3}$	$3.83x10^{-3}$	THF	100	100	52.8
$3.83x10^{-3}$	$3.83x10^{-3}$	OctMiMTfN	100	100	79.1

T= 80 °C, P= 30 bar, t= 3 h

In terms of aldehyde production, the solvent had no influence, since in the three of them the reaction was complete in 3 hours producing only aldehydes. However, the coordinating character of the solvent appeared to be an important factor in the formation of the linear aldehyde. In the highly polar and weakly coordinating OctMiMTfN the highest selectivity to linear aldehyde (79.1 %) was achieved. In an apolar non-coordinating solvent like toluene the catalyst performed in a similar manner to that observed in OctMiMTfN, since the selectivity to heptanal obtained was 74.9 %. Using a slightly polar solvent but highly coordinating like THF a large decrease of the production of heptanal relative to the other aldehydes was observed. In all cases 2-ethyl pentanal was produced, suggesting that the terminal alkene is isomerised to an internal position and the CO traps the branched Rh-alkyl formed. If the activation energy for the coordination of CO to the linear Rh-alkyl is low, it will be rapidly trapped leading to the linear aldehyde. In this case the l:b ratio is determined by the difference on the activation energy for the formation of the linear or branched

Rh-alkyl. However, if the activation energy for the coordination of CO to the linear Rh-alkyl is high, the equilibrium established between the two Rh-alkyl intermediates may revert to the resting state and form the branched Rh-alkyl. A large activation energy for the coordination of CO will favoured the formation of isomerised alkenes over the formation of the branched Rh-acyl to form the branched aldehyde.

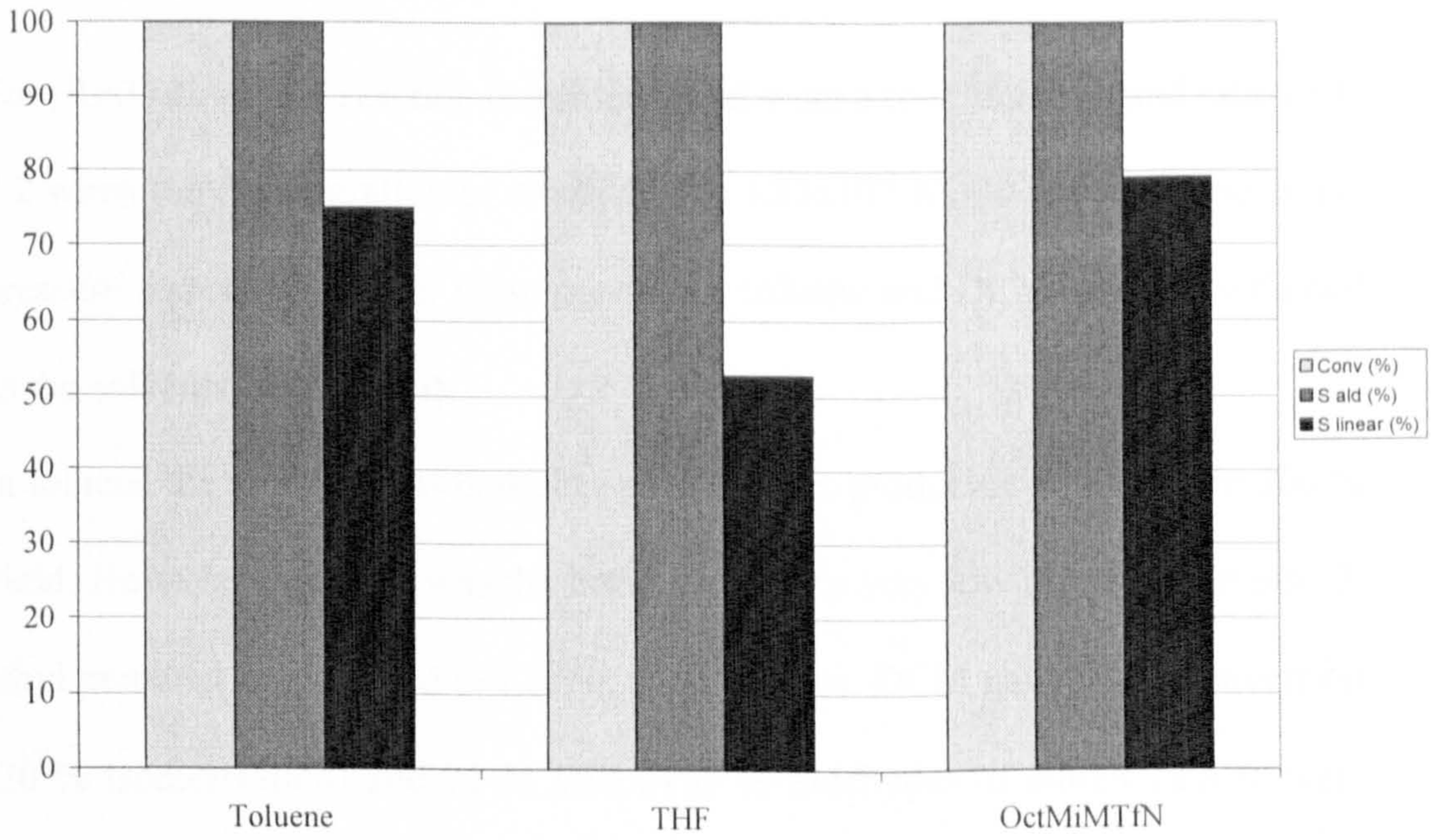


Figure 4- 2: Effect of different solvents on the hydroformylation of 1-hexene catalysed by $[RhCl(CO)_2]_2$ in the presence of DTBPMB.

4.2.1.2. $[Rh_2(OAc)_4]$as catalytic precursor.

$[Rh_2(OAc)_4]$ has been studied as a rhodium (II) precursor although it generally gives $[Rh(DTBPMB)H(CO)_2]$ under catalytic conditions and the effect of solvents, rhodium to DTBPMB ratio, the presence of a base and different ligands have been investigated. Table 4- 2 shows the results obtained.

Table 4- 2: Hydroformylation of 1-hexene with $[Rh_2(OAc)_4]$ and DTBPMB.

[Rh] (M)	[L] (M)	Solvent	T (°C)	P (bar)	Conv (%)	S ald (%)	S linear (%)
$3.83x10^{-3}$	$3.83x10^{-3}$	DCM	80	30	100	100	80
$3.83x10^{-3}$	$3.83x10^{-3}$	DCM(*)	80	30	100	100	72.8
$3.83x10^{-3}$	$8.46x10^{-3}$	DCM	80	30	98	78	77.9
$3.83x10^{-3}$	$8.46x10^{-3}$	Toluene	80	30	100	100	55.6

t= 3 h. (*): 0.14 mmol of NEt_3 added.

4.2.1.2.1. Effect of different solvents.

For $[Rh(OAc)_2]_2$ the reaction conditions used were a rhodium to ligand ratio of 1: 2.2 when the concentration of rhodium was $3.83x10^{-3}$ M, 30 bar of synthesis gas pressure and 80 °C. Under these conditions toluene and DCM were investigated as the solvents (*Figure 4- 3*).

In toluene the reaction was complete after 3 hours producing aldehydes in 100 % yield. However, not only was the linear selectivity very low (55.6 %) but also 2-ethyl pentanal was formed (11.3 %). Nevertheless, DCM gave 98 % conversion (20 % isomerisation) and 78 % selectivity to aldehydes of which 72.8 % were heptanal. In this case only 1.7 % of 2-ethyl pentanal was produced. These values suggest that in DCM isomerisation is not as effective as in toluene and that the hydroformylation of isomerised hexenes is partially inhibited in DCM, whereas in toluene this partial inhibition is not observed. Therefore the low linear selectivity observed in DCM may be due to a low selectivity in the formation of the linear Rh-alkyl.

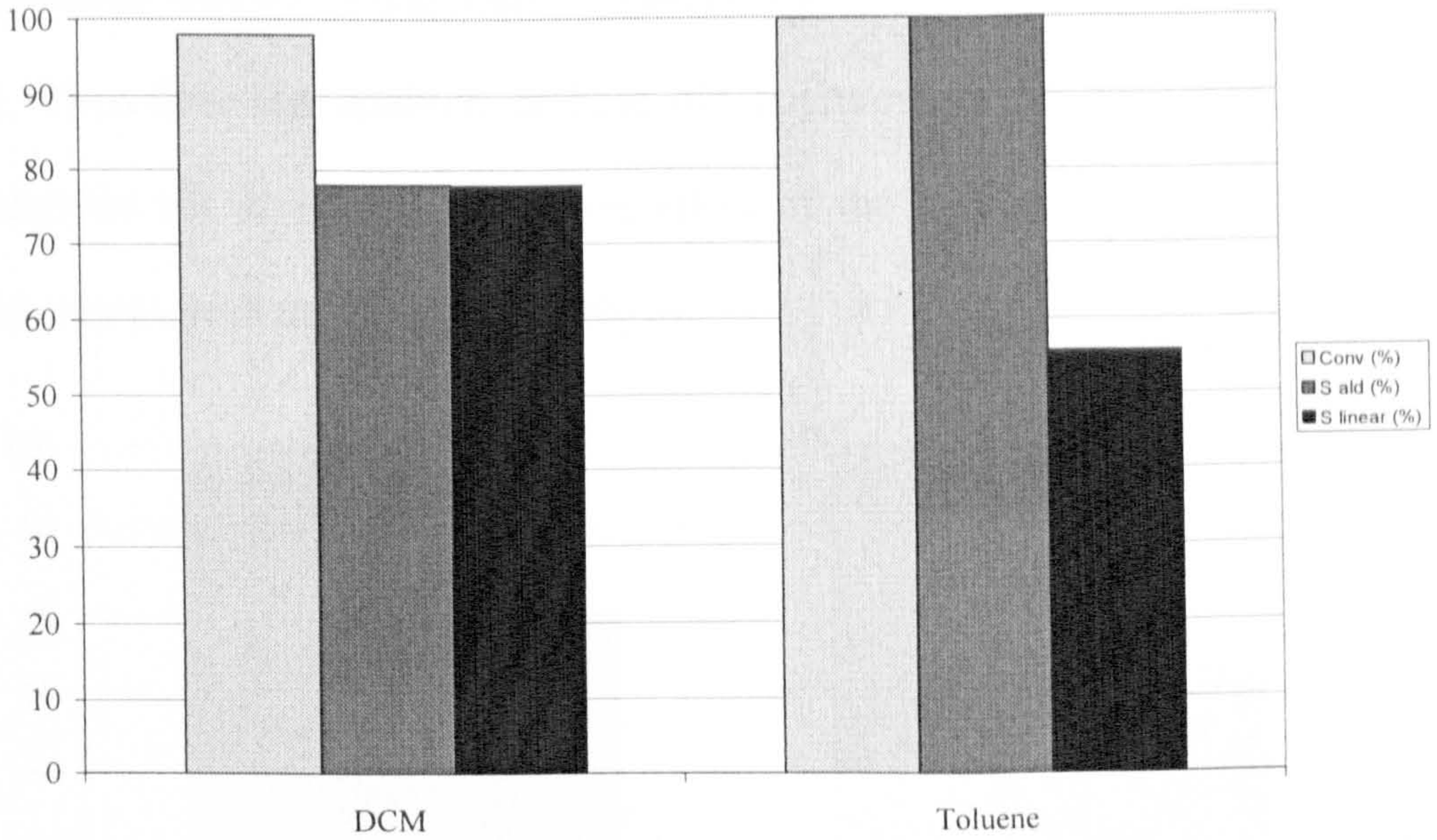


Figure 4- 3: Effect of different solvents on the hydroformylation of 1-hexene catalysed by [$Rh_2(OAc)_4$] and DTBPMB.

With DCM as the solvent, the Rh: ligand ratio was decreased from 1: 2.2 to 1: 1. As a result, a slight improvement on the selectivity to heptanal was achieved (80 %) and both conversion or selectivity to aldehyde were 100 % having inhibited the hydroformylation of internal hexenes, since only 1.1 % 2-ethyl pentanal was found.

4.2.1.2.2. Effect of addition of base.

The acetate groups contained in this rhodium precursor are lost in the presence of the diphosphine and hydrogen as acetic acid, which could affect the performance of the catalyst. Consequently and in order to neutralise the acid formed, a weak base, NEt_3, was added stoichiometrically to the solution, in which the Rh: ligand ratio was 1: 1. Although both the conversion and selectivity were 100 % in the presence and in the absence of NEt_3, a slight decrease of the production of linear aldehyde took place, since the selectivity to heptanal was only 72.8 % and 3.1 % of 2-ethyl pentanal was produced, whereas when no base was present the linear

selectivity was 80 % and 2-ethyl pentanal was formed in 1.1 % yield (*Figure 4-4*). Therefore, the addition of base did not promote the formation of linear aldehyde but it exerted promoting effect of the hydroformylation of internal hexenes to form the branched aldehyde.

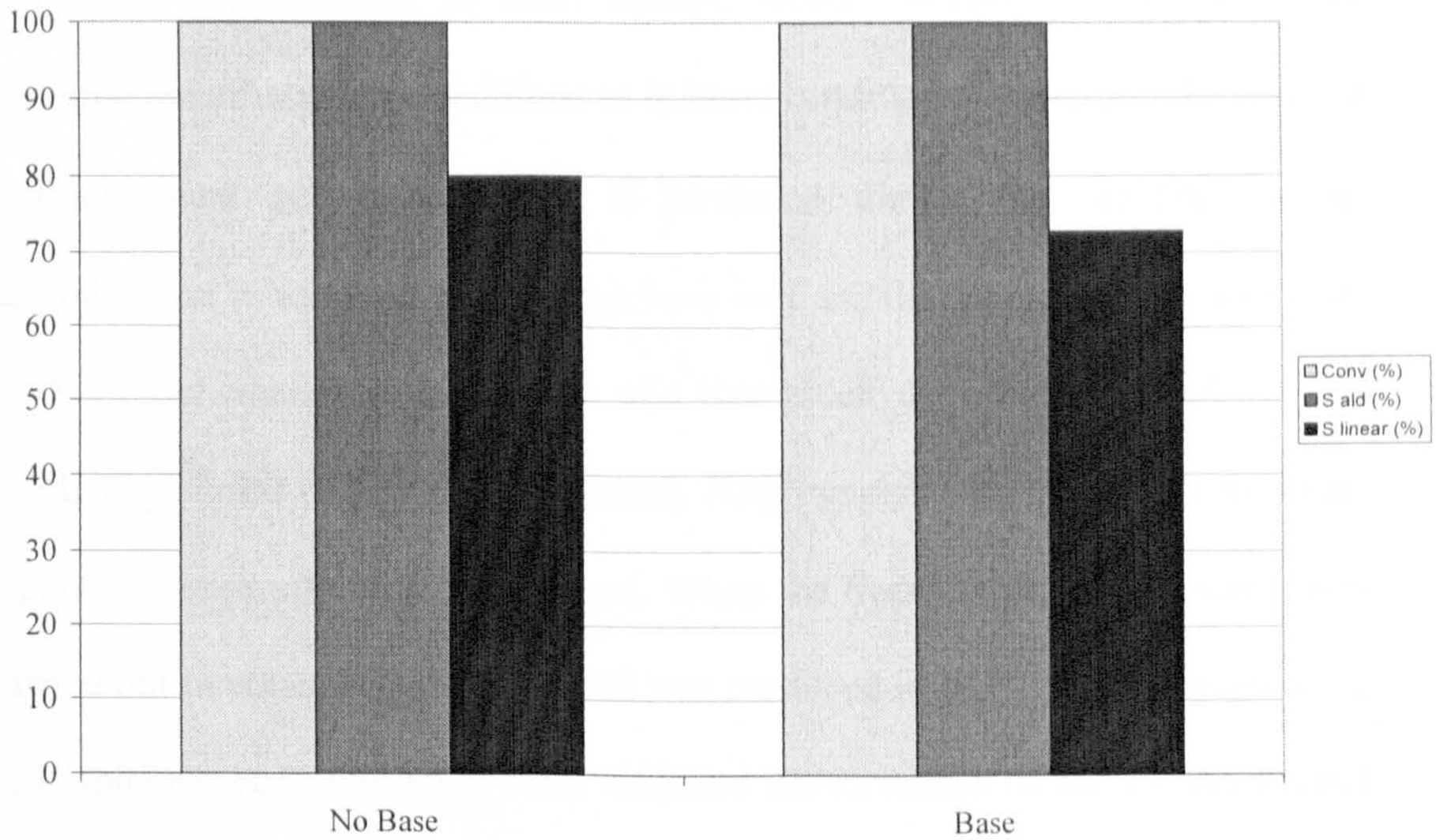


Figure 4- 4: Effect of addition of base on the hydroformylation of 1-hexene catalysed by $[Rh_2(OAc)_4]$ and DTBPMB.

4.2.1.3. $[RhCl_3 \cdot 3\ H_2O]$ as catalytic precursor.

The effectiveness of $[RhCl_3 \cdot 3H_2O]$ under the reaction conditions, [Rh]= [DTBPMB]= 3.83 x 10^{-3} M, 30 bar of CO:H_2, 80 °C in different solvents was studied.

4.2.1.3.1. Effect of the solvent.

This reaction was first attempted in DCM as the solvent. Although all the starting 1-hexene was consumed, only 72 % of the products obtained were aldehydes, of which only 22.4 % were linear. The high isomerisation observed (28 %) can be

attributed to the low solubility of [$RhCl_3 \cdot 3H_2O$]/ DTBPMB in DCM even after warming. [$RhCl_3 \cdot 3H_2O$] is only soluble in polar solvents such as alcohols or water. The disadvantage with the use of alcohols as solvents in hydroformylation reaction is the side reaction resulting from the nucleophilic addition of the alcohol to the aldehyde to form acetals. Acetal formation is known to be favoured either in acidic conditions or in basic conditions. Therefore, the reaction medium must be neutral. HCl is produced during the reaction, so its neutralisation is necessary and a weak base such as NEt_3 can do this. In a mixture of DCM and ethanol in the absence of a base aldehydes were produced in 97 % yield, 45 % linear (7 % 2-ethyl pentanal). Surprisingly, no acetals were observed. *Figure 4- 5* shows the results obtained. When the hydroformylation reaction was carried out in ethanol the linear acetal was produced in 83 % yield. The presence of a stoichiometric amount of NEt_3 inhibited the formation of acetals. As a result of the addition of base, complete conversion and 100 % selectivity to aldehyde (74 % linear) were achieved. In addition, only 1 % of 2-ethyl pentanal was recovered, suggesting that either the acetal formation or the hydroformylation of isomerised hexenes are partially inhibited. These conditions (EtOH/NEt_3) were the most effective for this catalytic system.

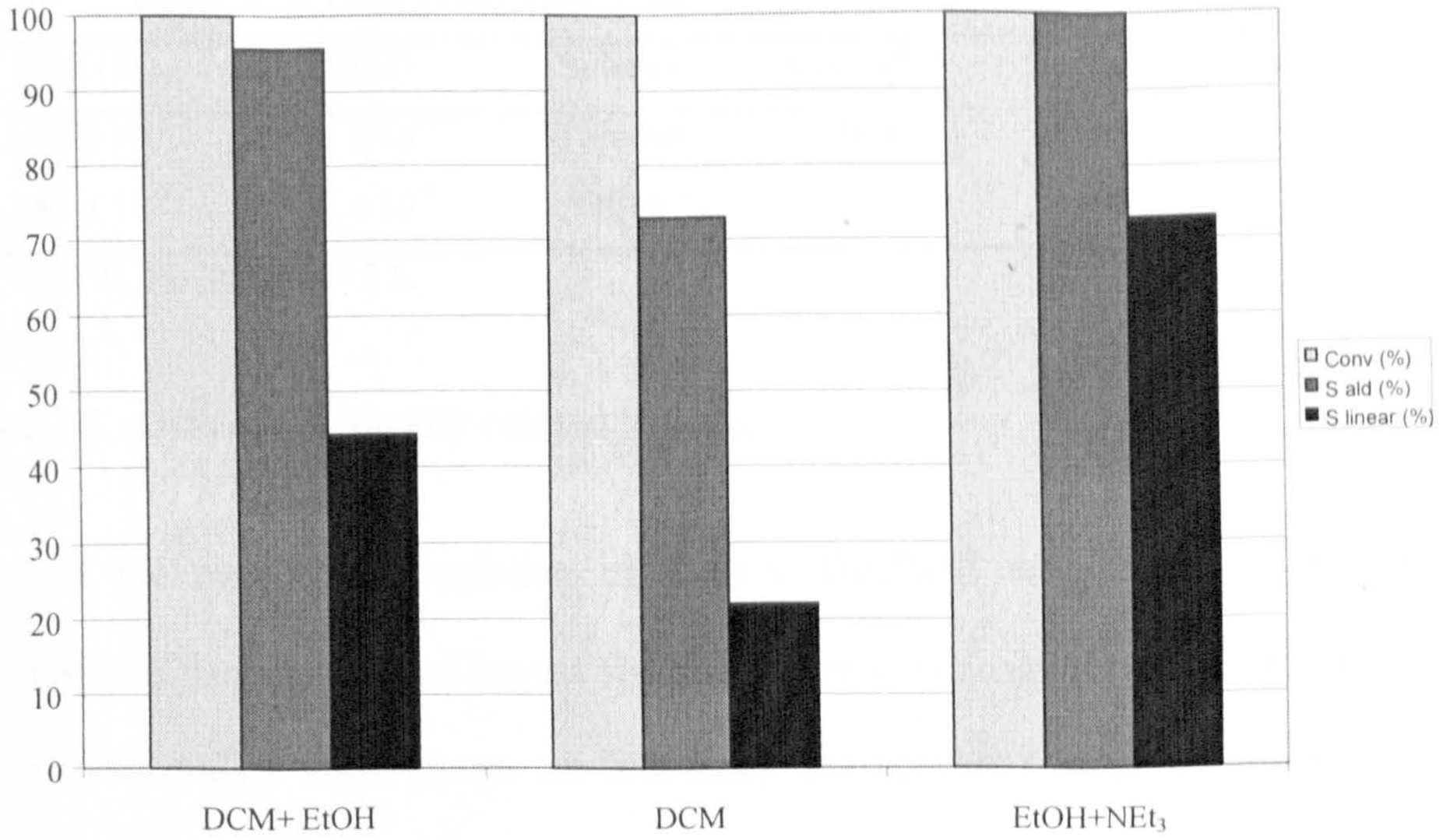


Figure 4- 5: Effect of solvents on the hydroformylation of 1-hexene catalysed by $[RhCl_3 \cdot 3H_2O]$ and DTBPMB.

4.2.1.4. [Rh(acac)(CO)$_2$] as catalytic precursor.

For [Rh(acac)(CO)$_2$] the influence of the solvent under the standard conditions of catalyst concentration, pressure and temperature was investigated. The solvents chosen were toluene and DCM (Table 4- 3). In both of them the reaction went to completion affording only aldehydes as products. A selectivity to linear aldehyde of 80 % was achieved in DCM, whereas in toluene it was only 58 %. The formation of 2-ethyl-pentanal in toluene (9 %) was more effective than in DCM (2 %), suggesting that in toluene isomerisation followed by hydroformylation occurs, whereas in DCM the tandem isomerisation-carbonylation is not favoured and a low selectivity in the formation of the linear Rh-alkyl is responsible for the low selectivity to the linear aldehyde.

Table 4- 3: Hydroformylation of 1-hexene with $[Rh(acac)(CO)_2]$

[Rh] (M)	[L] (M)	Solvent	Conv (%)	S ald (%)	S linear (%)
3.83×10^{-3}	3.83×10^{-3}	Toluene	100	100	58
3.83×10^{-3}	3.83×10^{-3}	DCM	100	100	80.4

T= 80 °C, P= 30 bar, t= 3 h.

4.2.1.5. Other structurally related ligands.

As in the methoxycarbonylation of alkenes, DIBPMB was used instead of DTBPMB. Isobutyl groups have a secondary carbon attached to the phosphorus atom. Secondary alkyl groups are less bulky and provide less steric hindrance than tertiary carbon atoms. Tolman introduced the cone angle to evaluate the steric bulk of monophosphines.[28] According to this concept the steric bulk of the monophosphines analogous to those considered for this study is: $^{i}Bu_3P$ <$^{t}Bu_3P$. Thus, bearing in mind that this term is defined for monophosphines, a correlation between $P^{t}Bu_3$/ $P^{i}Bu_3$ and DTBPMB/ DIBPMB could be carried out. Hence, the steric bulk of these bidentate phosphines would be: DIBPMB <DTBPMB. If the electron donating properties of these ligands are considered, the same order is found. It has been established that highly basic diphosphines lead to slow catalysts and also to low l:b ratios. Decreasing the basicity of the phosphine the back donation from the metal centre to the CO is decreased, making its dissociation easy and also facilitating the coordination of the alkene.

4.2.1.5.1. $[RhCl(CO)_2]_2$ as the rhodium precursor

As for the methoxycarbonylation of alkenes, 1,2-bis(di-*iso*-butylphosphinomethyl)benzene was used instead of the *tert*-butyl analogue. This

change meant a change in the electronic and in the steric properties and therefore a change in the catalysis was expected. Table 4- 4 displays the results obtained.

Table 4- 4: Effect of ligand.

[Rh] (M)	[L] (M)	Ligand	Solvent	Conv (%)	S ald (%)	S linear (%)
$3.83x10^{-3}$	$3.83x10^{-3}$	DTBPMB	Toluene	100	100	74.9
$3.83x10^{-3}$	$3.83x10^{-3}$	DIBPMB	Toluene	94.2	99.7	72.4

T= 80 °C, P= 30 bar, t= 3 h.

Using DIBPMB as the ligand only 94.2 % conversion was achieved after three hours, whereas with DTBPMB the reaction was complete. In addition, the selectivity to aldehydes and to the linear aldehyde were also lower for DIBPMB than for DTBPMB (*Figure 4- 6*). Moreover, 2-ethylpentanal was also formed more effectively showing that DIBPMB provides a good isomerisation catalyst and that the isomerised alkenes can be hydroformylated.

Iso-butyl groups are less electron donating than *tert*-butyl groups; therefore, the rhodium complex would be less electron rich. With regard to the steric properties, *iso*-butyl groups have the steric bulk further from the metal centre than *tert*-butyl groups. Thus, when DTBPMB is used as the ligand, the coordinated alkene will experience steric hindrance from the diphosphine and the most favourable position would be away from the ligand, leading to linear alkyl formation when hydride migration takes place.

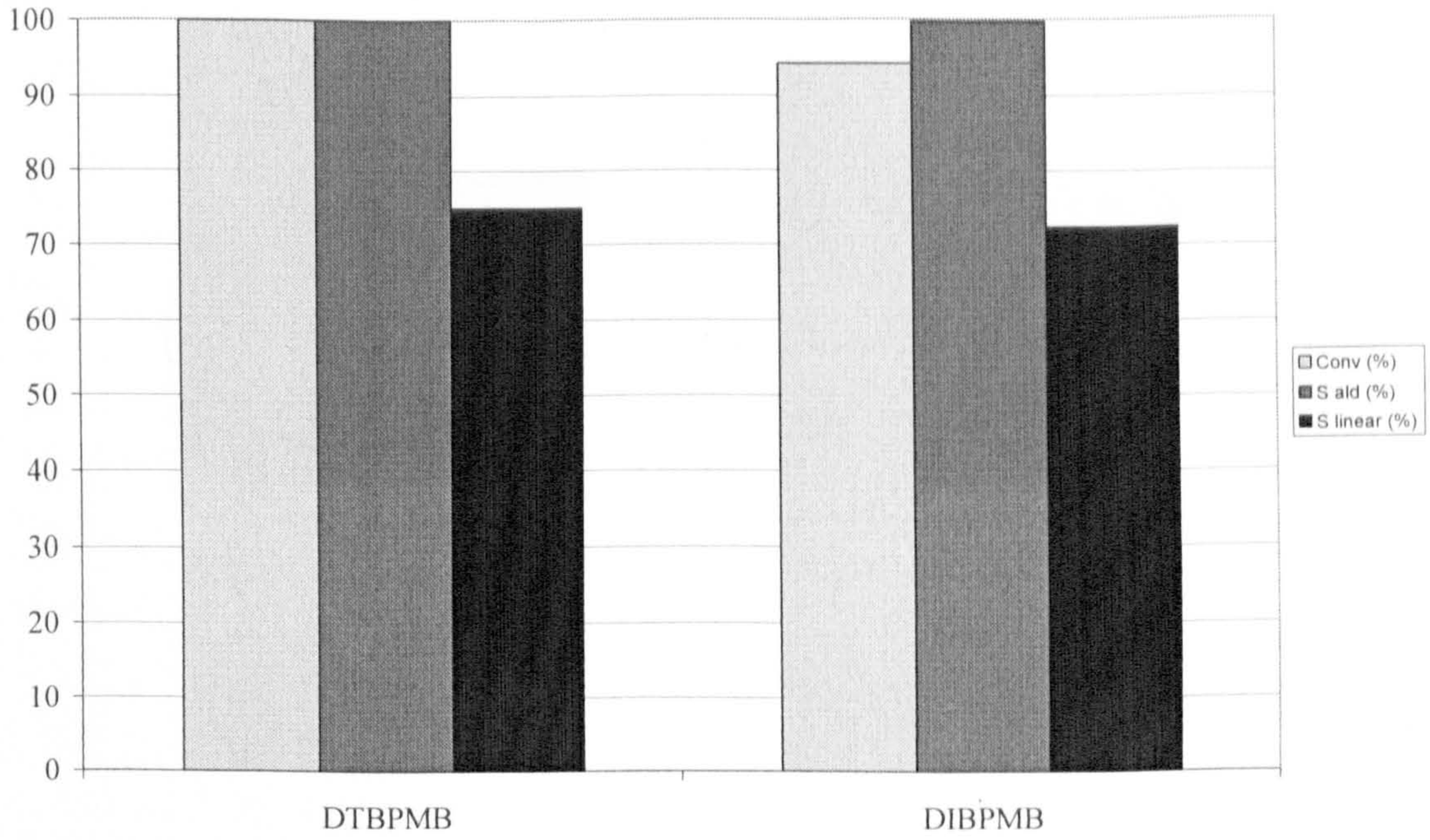


Figure 4- 6: Effect of different ligands on the hydroformylation of 1-hexene with $[RhCl(CO)_2]_2$.

4.2.1.5.2. $[Rh(OAc)_2]_2$ as the rhodium precursor.

The presence of further branched products was sought in order to see if the isomerisation effect observed for the system $[RhCl(CO)_2]_2$/ DIBPMB was also observed for the system $[Rh_2(OAc)_4]$/ DIBPMB. The three aldehydes (heptanal, 2-methyl-hexanal and 2-ethyl-pentanal) were present, as in the first case, but that 2-ethylpentanal was present in a larger amount. This suggests that the catalytic system made by $[Rh_2(OAc)_4]$/ DIBPMB is a better isomerisation catalyst than $[RhCl(CO)_2]_2$/ DIBPMB (*Figure 4- 7*).

The addition of NEt_3 did not improve the yield of the desired product. Once again DTBPMB turned out to be slightly more selective than DIBPMB under these conditions. The former produced aldehydes in 100 % yield (80 % linear) in a complete reaction after 3 hours. The latter converted 94.2 % of the starting material, producing aldehydes in 99.7 % selectivity (79.4 % linear).

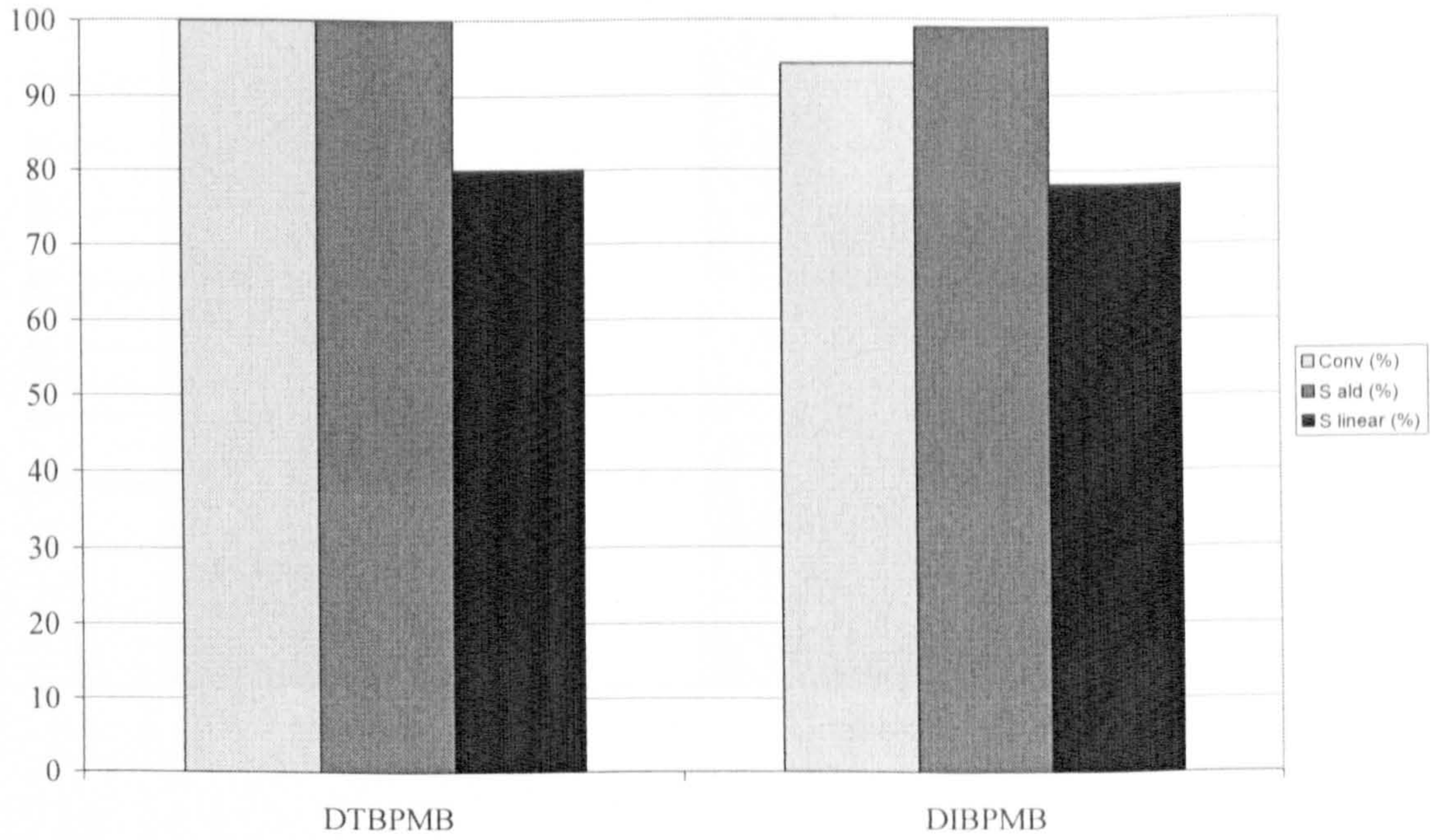


Figure 4- 7: Effect of different ligands on the hydroformylation of 1-hexene catalysed by $[Rh_2(OAc)_4]$ and DTBPMB.

4.2.1.5.3. $[RhCl_3 \cdot 3H_2O]$ as the rhodium precursor

As for the other two rhodium precursors, a comparative study of DTBPMB and DIBPMB was carried out using $[RhCl_3 \cdot 3H_2O]$ in ethanol. In the two experiments NEt_3 was added stoichiometrically to avoid the formation of acetals. This was successfully achieved when DTBPMB was used but surprisingly it was not when DIBPMB was used. The latter gave acetals in 28 % yield and aldehydes in 72 % yield, from which 71 % were the desired heptanal (*Figure 4- 8*).

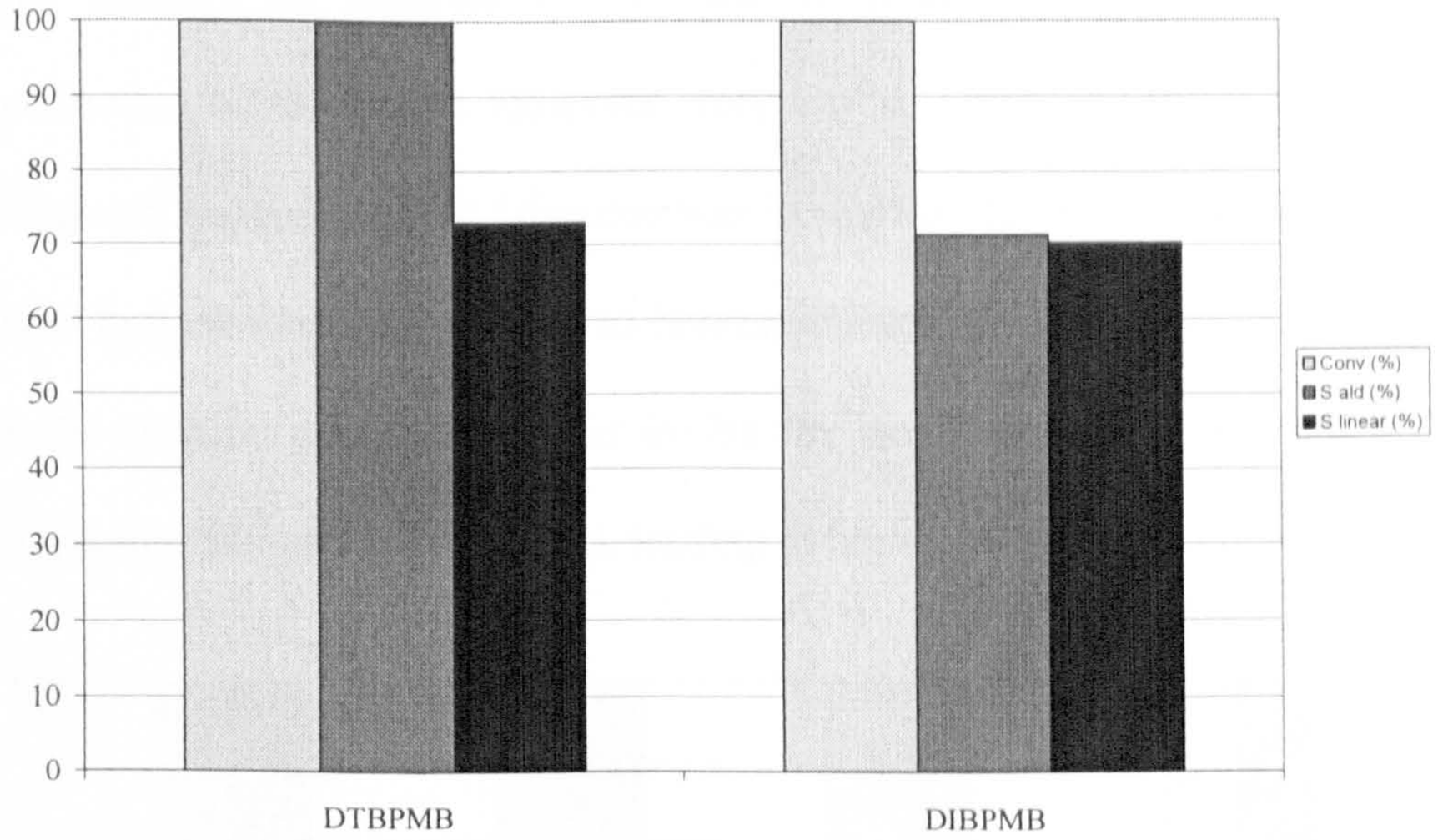


Figure 4- 8: Effect of different ligands on the hydroformylation of 1-hexene catalysed by [$RhCl_3 \cdot 3\ H_2O$].

4.2.1.6. Comparison of the four different rhodium precursors.

As a general view, the best results obtained with the different rhodium precursors are shown in *Figure 4- 9*.

It must be noted that the four systems showed contain chlorine, either in the solvent or as part of the starting rhodium precursor. For these rhodium-chloride complexes Wilikinson reported in the sixties only partial conversion to hydrido species, which may lead to erroneous results.

In all the cases presented a compromise between conversion and selectivity was achieved, reaching reasonably high selectivity with high conversion. However, the systems formed by [$Rh(acac)(CO)_2$]/ DCM and by [$RhCl(CO)_2]_2$/ toluene gave the most balanced results. These data reveal that the presence of chlorine in the reaction medium plays an important role in the isomerisation-hydroformylation reaction, inhibiting the hydroformylation of internal double bonds and therefore favouring the selective formation of linear aldehydes.

The absence of chlorine in the reaction medium very much favours the production of aldehydes. However, very low selectivity to linear aldehyde was observed, suggesting that 1-hexene was isomerised to internal hexenes and these were hydroformylated, leading to branched aldehydes. The presence of chlorine in the reaction medium does not inhibit the isomerisation but hydroformylation of internal alkenes is suppressed, leading to higher selectivity to linear.

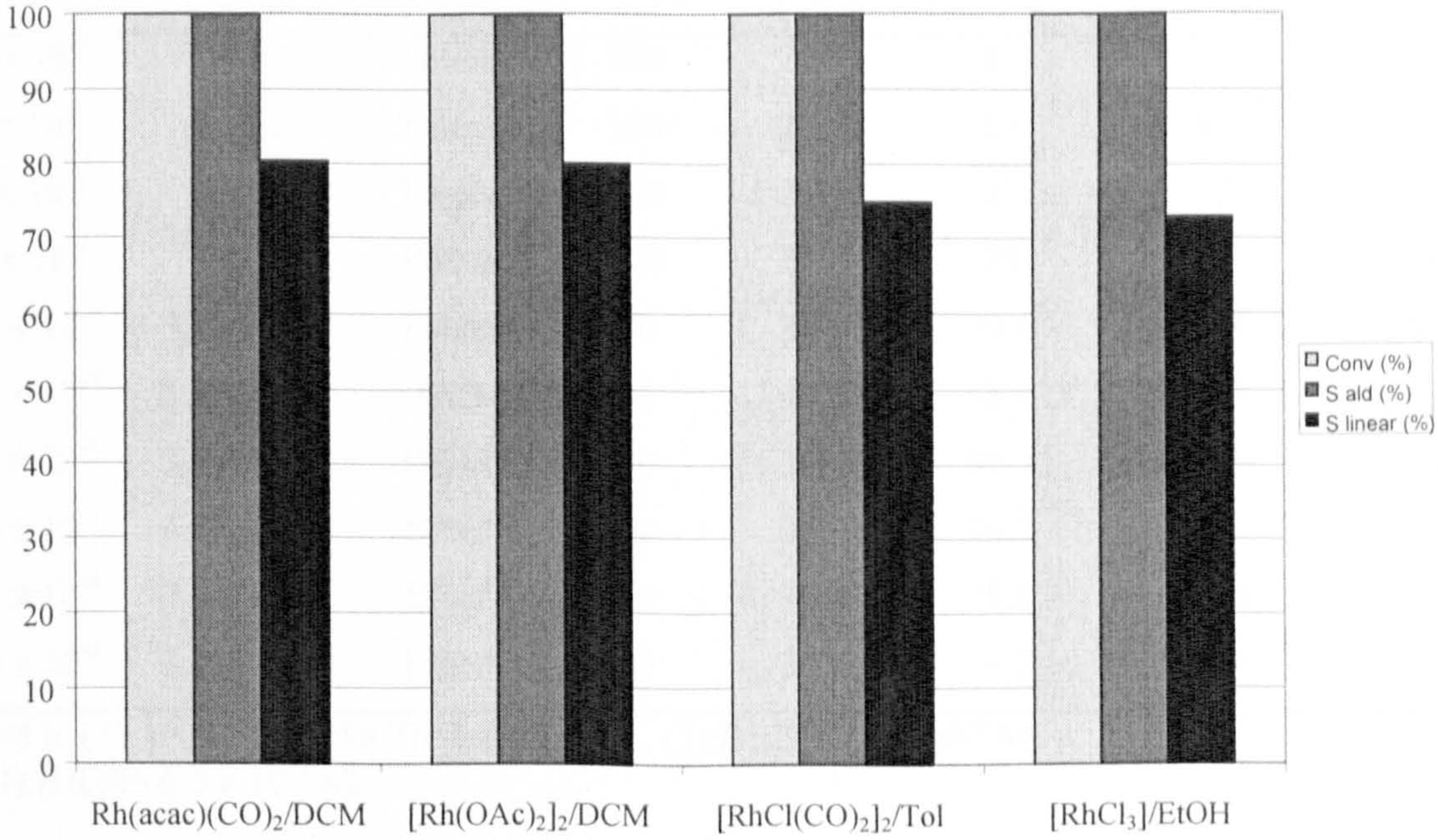


Figure 4- 9: Comparison of four different rhodium precursors.

4.2.2. Hydroformylation of 1-octene.

Following the promising results obtained for 1-hexene, the same systematic approach was taken to the study of the rhodium catalysed hydroformylation of 1-octene. Using different rhodium precursors, reactions were performed in which [Rh], solvent, base, temperature, pressure, and reaction time were varied.

4.2.2.1. [Rh(acac)(CO)$_2$]as catalytic precursor.

[Rh(acac)(CO)$_2$] is the most widely used rhodium precursor for hydroformylation reactions. Different solvents, concentrations and different conditions of pressure and temperature have been studied (Table 4- 5).

Table 4- 5: Hydroformylation with Rh(acac)(CO)$_2$

[Rh} (M)	[L] (M)	Solvent	T (°C)	P (bar)	Conv (%)	S ald (%)	S linear (%)
2.5×10^{-3}	5×10^{-3}	Toluene	100	20	84	75	63
2.5×10^{-3}	0.013	Toluene	100	20	13	65	10
2.5×10^{-3}	0.013	Toluene	120	20	43	72	31
2.5×10^{-3}	0.013	Ethanol	120	20	70	71	49
3.83×10^{-3}	3.83×10^{-3}	Toluene	80	30	99.8	92.4	48.3
3.83×10^{-3}	3.83×10^{-3}	DCM	80	30	98.4	28.8	82.3
3.83×10^{-3}	3.83×10^{-3}	DCM[(1)]	80	30	99.7	94	59.0
3.83×10^{-3}	3.83×10^{-3}	Ether[(2)]	80	30	99.7	79.5	69.0
3.83×10^{-3}	3.83×10^{-3}	Ether[(3)]	80	30	99.8	93.8	60.8
3.83×10^{-3}	3.83×10^{-3}	Ether[(4)]	80	30	40.3	34.9	75.7

t=3 h. (1): t=18 h. (2):[HCl]= 1.9×10^{-3} M. (3):[HCl]= 3.8×10^{-3} M.
(4):[HCl]= 6.7×10^{-3} M.

4.2.2.1.1. Effect of the solvent.

Using [Rh(acac)(CO)$_2$] as the catalytic precursor the influence of the solvent was investigated. The reaction conditions used were: (1) reaction temperature of 120 °C and concentration of rhodium of 2.5×10^{-3} M and concentration of diphosphine of 0.013 M (*Figure 4- 10*), and (2) reaction temperature of 80°C and concentration of rhodium and diphosphine of 3.83×10^{-3} M (*Figure 4- 11*).

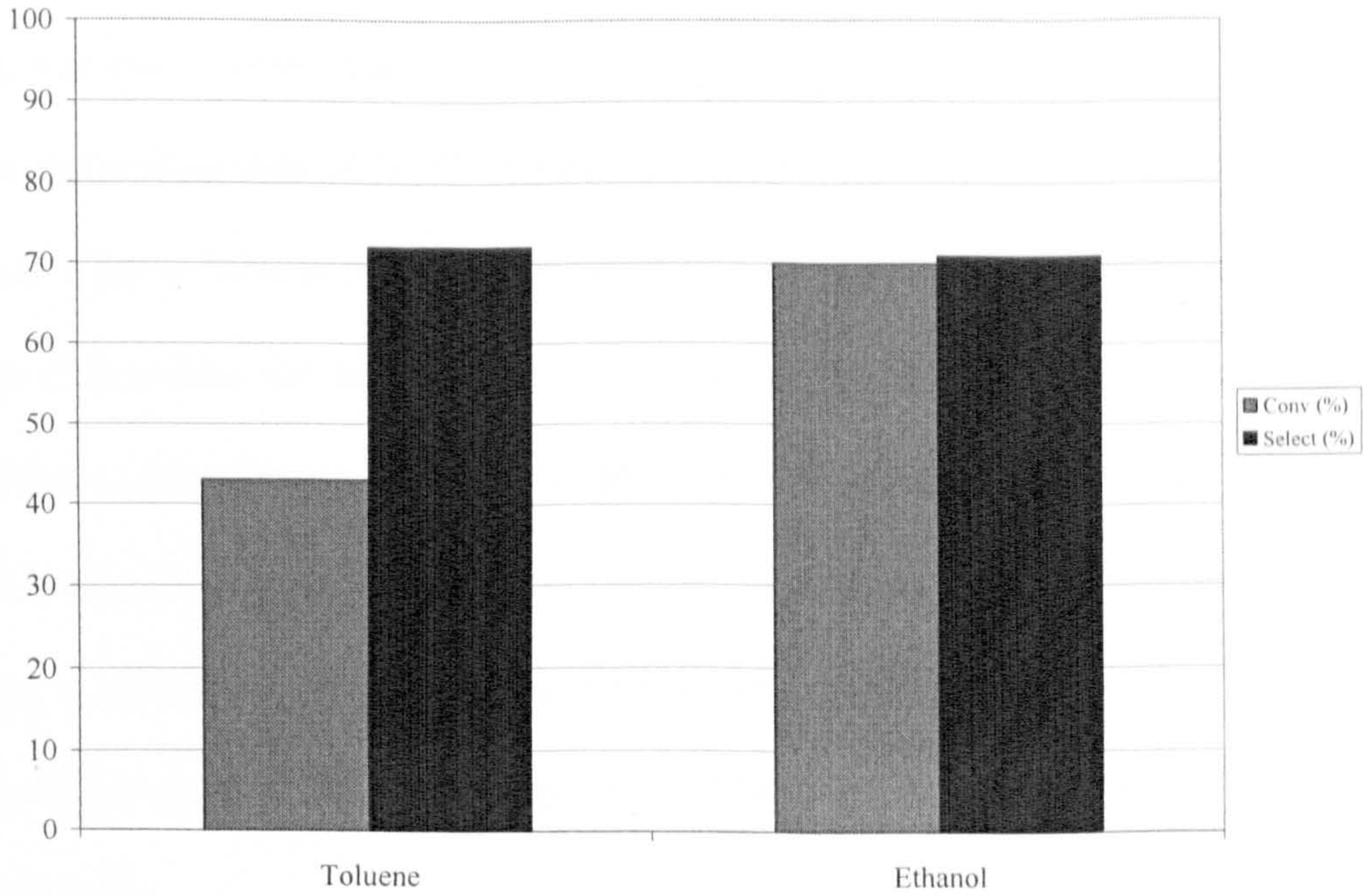


Figure 4- 10: Effect of the solvent on the hydroformylation of 1-octene catalysed by [Rh(acac)(CO)$_2$] and DTBPMB at 120°C.

In toluene at 120 °C and under reaction conditions (1) poor conversion to aldehydes was achieved (43 %), whereas in ethanol aldehydes were formed in 70 % yield. The selectivity to aldehydes obtained in both cases was similar (~70 %) and the selectivity to linear aldehyde was slightly higher in ethanol (49 %) than in toluene (31 %). No alcohols were formed in the latter case, despite the fact that their production is favoured by the presence of protic solvents and highly electron donating ligands.[21]

In DCM at 80 °C and under reaction conditions (2) the yield of aldehydes was 28 % after 3 hours. Isomerisation occurred faster than in toluene, since only 3 % of 1-octene was recovered at the end of the reaction (69 % isomerised alkenes). This prompted us to investigate more deeply the relation between low aldehyde formation and high selectivity to linear aldehyde. The reaction time was increased to 18 hours to promote a high conversion. Not only were the selectivity to aldehydes and the selectivity to linear aldehyde higher in DCM than in

toluene, but also 2-ethyl heptanal was found in smaller amount in DCM than in toluene, suggesting that in DCM hydroformylation of internal alkenes is partially inhibited. This is further evidence of the positive effect of a chlorinated solvent vs a non-chlorinated for the selective hydroformylation of terminal alkenes.

The lower conversions observed under reaction conditions (1) than those observed under reaction conditions (2) are in agreement with the accepted rate equation in which an increase on the concentration either of rhodium or alkene leads to a fast reaction, whereas an increase on the concentration of phosphine or CO inhibits it.

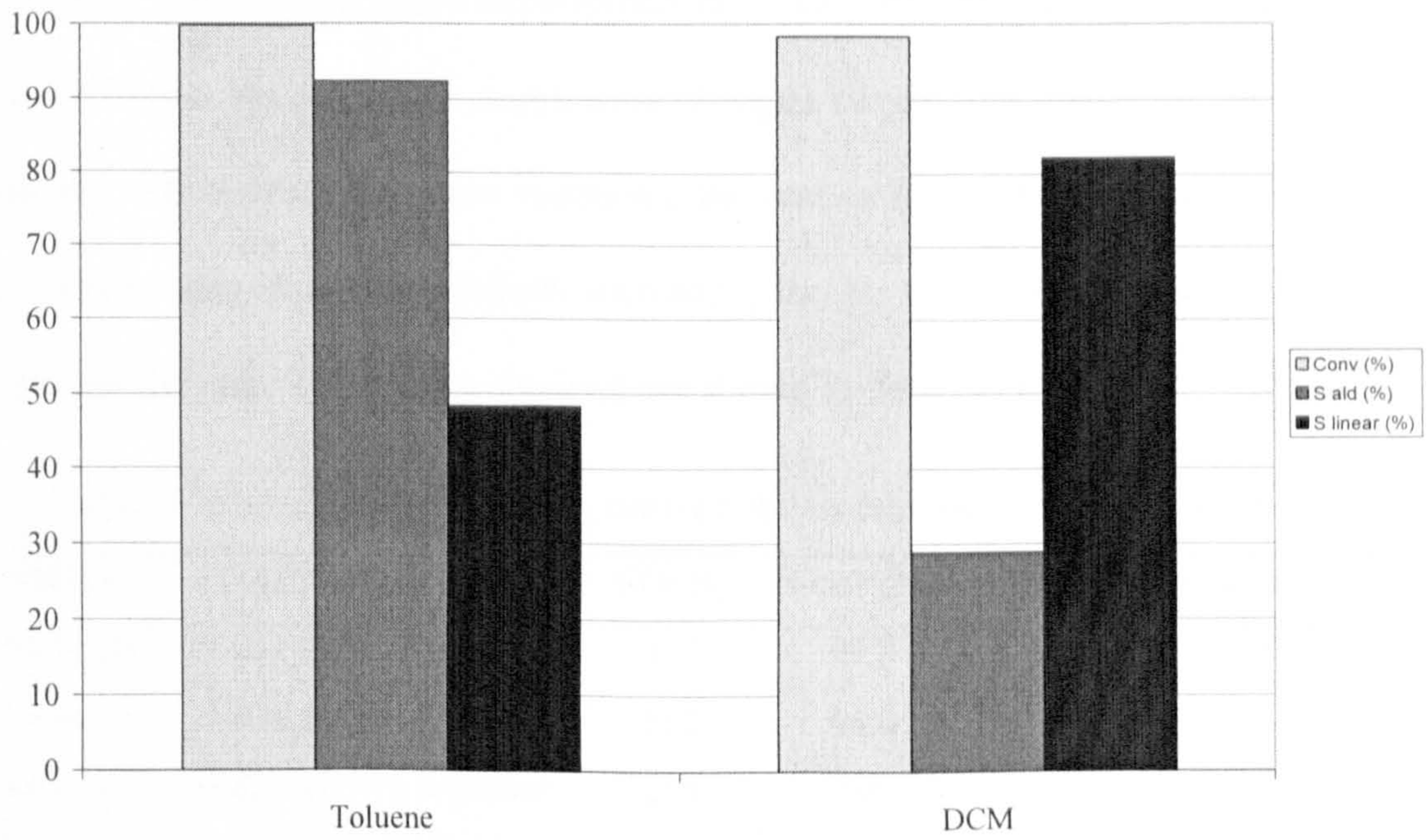


Figure 4- 11: Effect of the solvent on the hydroformylation of 1-octene catalysed by [Rh(acac)(CO)$_2$] and DTBPMB at 80 °C

When the solvent was ether, HCl was the chlorine source. Adding it stoichiometrically (Table 4- 5) very little isomerised alkenes were formed, so that high selectivity to aldehydes was observed (93.8 %) and nonanal was produced in 60.8 % yield. By reducing the amount of HCl added the total amount of

aldehydes produced decreased to 79.5 %, although higher selectivity to linear produced was obtained (69 %). Further addition of HCl exerts an inhibiting effect on the hydroformylation reaction with mainly 1-octene being recovered after the reaction.

4.2.2.1.2. Effect of CO: H_2 ratio.

The effect of the CO: H_2 ratio has been studied using a polar solvent and an apolar solvent. If the rate determining step were the oxidative addition of dihydrogen, an increase of the partial pressure of H_2 would lead to a faster reaction. However, in these experiments the total pressure was kept constant, so both CO and H_2 partial pressures were changed in opposite directions. In most, but not all, hydroformylation reactions, the rate is first order in hydrogen and negative order in CO. Therefore, increasing the H_2 to CO ratio is expected to increase the rate. The results obtained are shown in Table 4- 6.

Table 4- 6: Effect of the CO: H_2 ratio on the hydroformylation of 1-octene

[Rh](M)	[L] (M)	Solvent	CO: H_2	Conv (%)	S ald (%)	S linear (%)
3.83×10^{-3}	3.83×10^{-3}	Toluene	1: 1	99.8	92.4	48.3
3.83×10^{-3}	3.83×10^{-3}	Toluene	1: 2	66.6	60.2	76.3
3.83×10^{-3}	3.83×10^{-3}	Toluene	2: 1	100	43.2	45.1
3.83×10^{-3}	3.83×10^{-3}	^{t}BuOH	1: 1	86.8	70.6	73.1
3.83×10^{-3}	3.83×10^{-3}	^{t}BuOH	1: 2	62.4	58	72.4
3.83×10^{-3}	3.83×10^{-3}	^{t}BuOH	2: 1	100	98.8	54.3

T= 80 °C, P= 30 bar, t= 3h.

In ^{t}BuOH an increase in the partial pressure of CO (decrease in the partial pressure of H_2) leads to higher selectivity to aldehydes and an increased rate of reaction. Thus, in contrast to what was expected, a high partial pressure of CO seems to increase the rate. This could be explained, if the coordination or

insertion of CO were rate determining. This is sometimes observed in other systems. A lower linear selectivity is observed at the higher partial pressure of CO. This appears to be associated with the higher selectivity to aldehydes and suggests that the branched Rh-alkyl is preferentially carbonylated at high P_{CO} but undergoes β-hydrogen abstraction at lower P_{CO}, leading to isomerised alkenes, lower aldehyde selectivity and higher linear selectivity.

A similar trend is seen in toluene except that at high P_{CO}, the reaction gives low selectivity to aldehydes and lower linear selectivity. This may suggest that a different active species, perhaps with the DTBPMB bound through only one phosphorus atom, is present. The single coordinated phosphine would be expected to give much lower selectivity to linear aldehyde and may give lower rates of hydroformylation compared with isomerisation. This is what is observed.

4.2.2.1.3. Effect of Rh: L ratio.

In order to increase the catalyst stability, the rhodium to ligand ratio was increased from 1: 1 to 1:10. Table 4- 7 and *Figure 4- 12* illustrate the results obtained.

Table 4- 7: Effect of Rh: L in the hydroformylation of 1-octene

[Rh](M)	[L] (M)	Rh: L	Conv (%)	S ald (%)	S linear (%)
$3.25x\ 10^{-3}$	$3.25x\ 10^{-3}$	1: 1	99.7	86.4	42.1
$3.25x\ 10^{-3}$	$6.5x\ 10^{-3}$	1: 2	99.7	88.8	54
$3.25x\ 10^{-3}$	$9.75x\ 10^{-3}$	1: 3	59.1	61.8	68.5
$3.25x\ 10^{-3}$	$13x\ 10^{-3}$	1: 4	59	65.8	64.4
$3.25x\ 10^{-3}$	$16.2x\ 10^{-3}$	1: 5	99.8	92.5	47.9
$3.25x\ 10^{-3}$	$32.5x\ 10^{-3}$	1: 10	49.7	42.5	77.7

T= 80 °C, P= 30 bar, t= 3h, solvent= DCM.

On going from 1: 1 ratio to 1: 2 the conversion of 1-octene remained >99 %, the selectivity to aldehydes increased slightly and the linear aldehyde was produced in higher yield. Further increase from 1: 2 to 1: 3 and 1: 4 produced a great inhibition of the reaction. However and surprisingly, when the ratio used was 1: 5, the activity increased and the highest level of linear aldehyde was observed. No further improvement was reached by increasing the ligand: Rh ratio to 10: 1. In addition, a black precipitate (presumed to be rhodium metal) could be observed at the end of the reaction. Thus, the lower activity can be attributed to the decomposition of the complex. These findings can also be explained considering the rate equation in which a high concentration of phosphine has a negative effect in the rate. Many similar studies have shown that hydroformylation reactions are negative order in phosphine.[30]

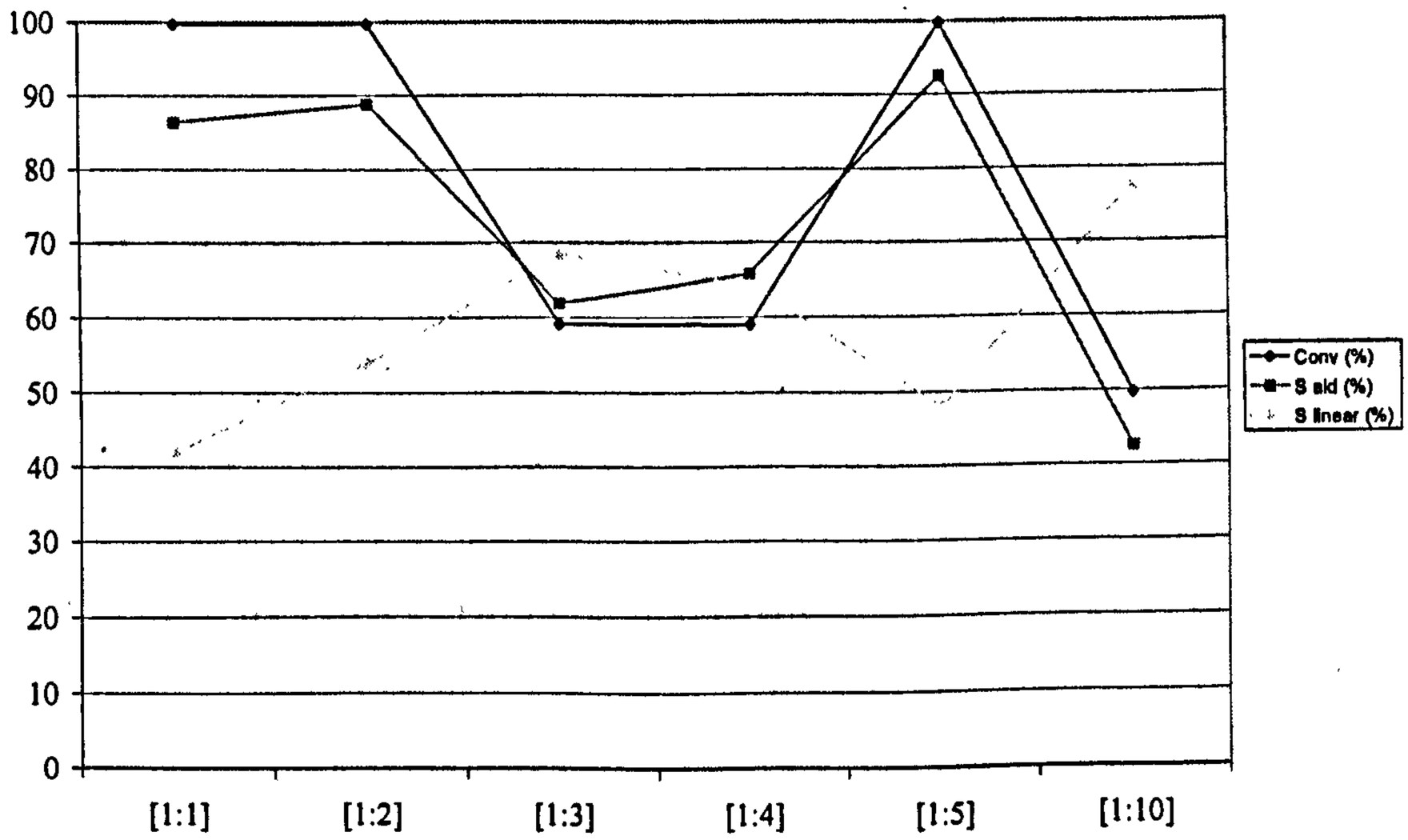


Figure 4- 12: Influence of Rh: L ratio on hydroformylation of 1-octene catalysed by [Rh(acac)(CO)2] and DTBPMB.

For example, Unruh and co-workers studied the effect of P: Rh ratio on the selectivity towards the linear aldehyde for the dppf-Rh system. They found the

highest selectivity towards the linear aldehyde when the ligand to rhodium ratio was 1.5: 1. Increasing this ratio to 3: 1 did not improve the results. Consequently, they proposed that 3 species are in equilibrium, but also that the dimeric species shown in *Figure 4- 13* was the most selective.[15] Alkene coordination to these dimeric species requires the dissociation of one of the phosphorus atoms bounded to the metal centre, which is especially difficult at high phosphine concentration.

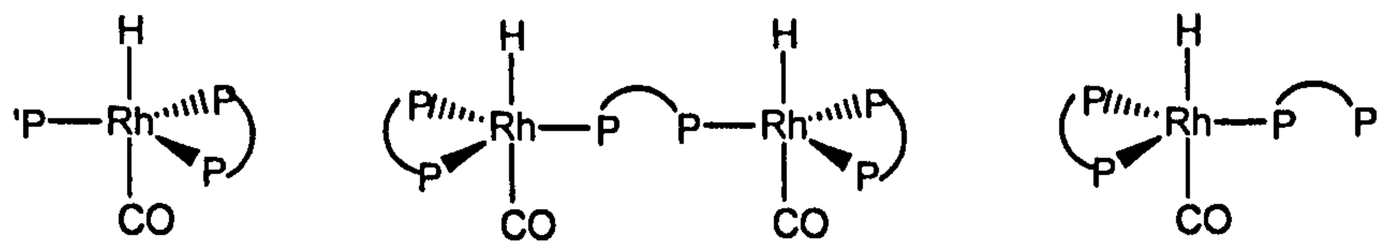


Figure 4- 13: Rhodium species in equilibrium under CO-H_2 for P-P= dppf

However, van Leeuwen showed for trixantphos that these species are not feasible due to the rigid nature of the ligand and to the readily displacement of the third phosphine under CO atmosphere. They attributed the optimum ligand to rhodium ratio to the result of a dissociation equilibrium between rhodium species containing the ligand coordinated in a bidentate mode and rhodium species containing the ligand coordinated in a unidentate fashion.[24]

4.2.2.2. $[RhCl(CO)_2]_2$ as catalytic precursor.

For this rhodium precursor the concentration of rhodium and DTBPMB were kept constant throughout, varying parameters such as solvent, concentration, CO: H_2 ratio and pressure. The results obtained are shown in Table 4- 8.

Table 4- 8: Hydroformylation of 1-octene using $[RhCl(CO)_2]_2$ as rhodium precursor

[Rh](M)	[L] (M)	Solvent	P (bar)	Conv (%)	S ald (%)	S linear (%)
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	30	99.1	67.9	60.9
$3.83x10^{-3}$	$3.83x10^{-3}$	DCM	30	97.3	70.6	63.1
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene(1)	30	99.7	80.9	67
$3.83x10^{-3}$	$3.83x10^{-3}$	DCM(1)	30	99.5	82.8	76.3
$3.83x10^{-3}$	$3.83x10^{-3}$	MeOH	30	98	2	75
$3.83x10^{-3}$	$3.83x10^{-3}$	^{t}BuOH	30	99	58.2	41.7
$3.83x10^{-3}$	$3.83x10^{-3}$	OctMiMTfN	30	25.3	6.4	77.1

T= 80°C, t= 3h. (1): t= 18 h.

4.2.2.2.1. Effect of the solvent

The performance of this catalytic system in several solvents, such as toluene, DCM, MeOH, ^{t}BuOH and OctMiMTfN was explored when 1-octene was used as the substrate (*Figure 4- 14*).

For the hydroformylation of 1-octene in toluene and in DCM the values for selectivity to aldehydes were lower than for 1-hexene, 67.9 % and 70.6 % respectively. This suggests that whilst the length of the alkene increases the rate of isomerisation increases and the rate of hydroformylation decreases. In order to check the generality of the positive effect of the chlorine observed for the hydroformylation of 1-hexene, high conversion to aldehydes was promoted by increasing the reaction time in both solvents (toluene and DCM). The levels of isomerisation achieved in DCM (16.7 %) were lower than in toluene (18.8 %). However, the selectivity to aldehydes in DCM (82.8 %) was higher than in toluene (80.9 %) and so was the linear selectivity, 76.3 % in DCM and 67 % in toluene. The product arose from the tandem isomerisation-hydroformylation, 2-ethyl heptanal, was formed in 7.5 % yield in toluene and in 2 % yield in DCM. These findings are in agreement with our previous findings and provide further

evidence of the partial inhibition of the tandem isomerisation-carbonylation reaction promoted by DCM to lead to higher linear selectivity than in a non chlorinated solvent when a non chlorinated rhodium precursor is used.

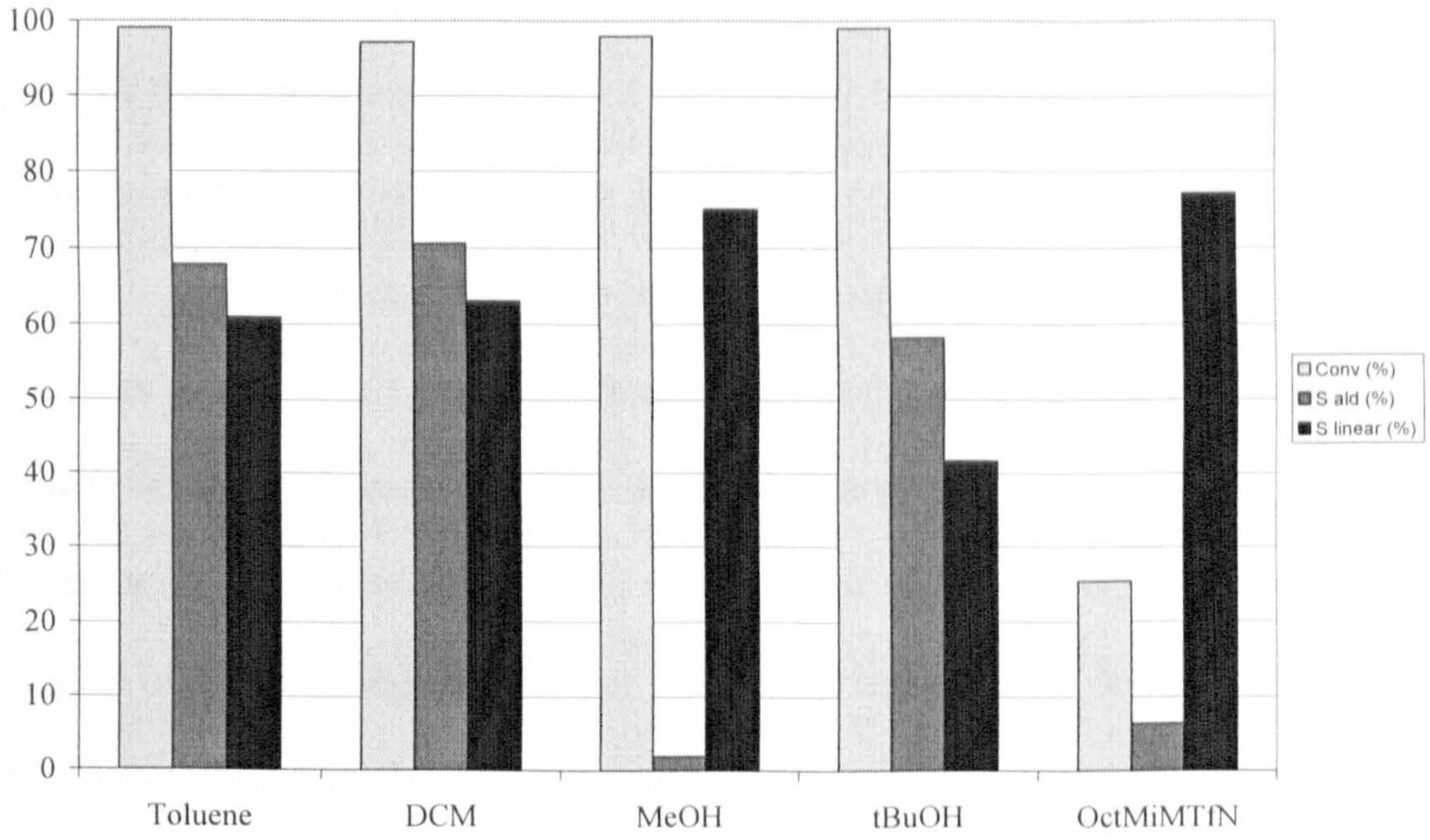


Figure 4- 14: Effect of different solvents on the hydroformylation of 1-octene catalysed by $[RhCl(CO)_2]_2$ and DTBPMB.

The conversion to aldehydes was very low when MeOH or OctMiMTfN were used (2 % for MeOH and 6.4 % for OctMiMTfN), although selectivities to linear aldehyde were >75 % in both cases. In ^{t}BuOH, 58.2 % yield of aldehydes was achieved, with a linearity of 41.7 %. The use of alcohols as solvents favours the formation of acetals as side products. In the case of MeOH, 12% of the products formed were acetals (88 % linear), whereas when ^{t}BuOH were used, no acetal formation took place despite its high nucleophilicity suggesting that the steric bulk of the *tert*-butoxide ion hinders the nucleophilic attack onto the aldehyde.

A decrease in the selectivity seems to occur when the conversion increases. This effect is not unusual and can be attributed to increased levels of alkene isomerisation followed by hydroformylation of the internal alkene so formed to

give branched aldehydes. In support of this, an increase on the isomerised octenes takes place when the conversion increases, as shown in Table 4- 8.

4.2.2.2.2. Effect of the pressure.

Initial CO: H_2 pressures were varied from 10-60 bar and the results of these reactions can be observed in Table 4- 9 and *Figure 4- 15*.

Under 10 bar the reaction is much slower than at 30, 45 and 60 bar giving aldehydes in 11.2 %, 67.9 %, 69.5 % and 95 % yield, respectively. With regard to the selectivity to linear aldehyde, the values observed decreased on going from 10 bar to 45 bar but increased again under 60 bar of CO-H_2. Under 10 bar of pressure of CO-H_2, when 88.8 % of isomerised octenes were formed, 100 % selectivity to linear aldehyde was obtained.

Table 4- 9: Effect of pressure in the hydroformylation of 1-octene with $[RhCl(CO)_2]_2$

[Rh](M)	[L] (M)	Solvent	P(bar)	Conv (%)	S ald (%)	S linear (%)
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	10	100	11.2	100
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	30	99.1	67.9	60.6
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	45	100	69.5	40.3
$3.83x10^{-3}$	$3.83x10^{-3}$	Toluene	60	100	95	57.9

T= 80 °C, t= 3 h.

An increase of the pressure from 30 to 45 and to 60 bar had a great effect on the selectivity, since at 30 bar 60.6 % selectivity to nonanal was achieved, at 45 bar the selectivity to nonanal was 40.3 % and at 60 bar this product was obtained in 57.9 % selectivity.

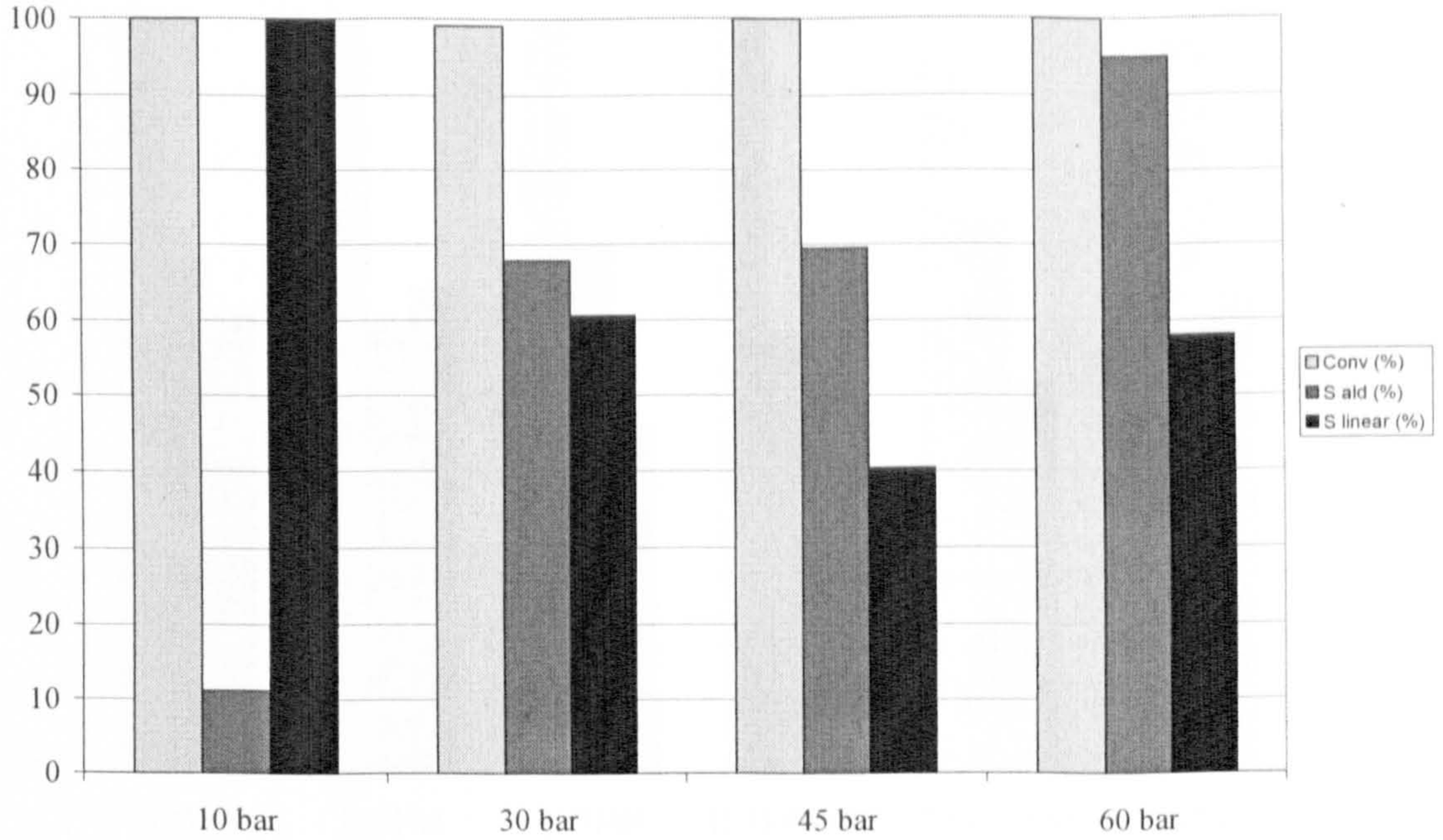


Figure 4- 15: Effect of pressure on the hydroformylation of 1-octene catalysed by $[RhCl(CO)_2]_2$ and DTBPMB

4.2.2.2.3. Effect of the CO: H_2 ratio.

To gain understanding of how the partial pressure of each of the two gases affects the hydroformylation reaction, the effect of the CO: H_2 ratio was examined. The outcome of this set of experiment is shown in *Figure 4- 16* and Table 4- 10.

Table 4- 10: Effect of the CO: H_2 ratio in the hydroformylation of 1-octene

[Rh](M)	[L] (M)	Solvent	CO: H_2	Conv (%)	S ald (%)	S linear (%)
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	Toluene	1: 1	99.1	67.9	60.9
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	Toluene	1: 2	99.3	59.3	64
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	Toluene	2: 1	99.5	70.2	45.6
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	^{t}BuOH	1: 1	99	58.2	41.7
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	^{t}BuOH	1: 2	98.9	72.6	51.8
$3.83x\ 10^{-3}$	$3.83x\ 10^{-3}$	^{t}BuOH	2: 1	98.1	98	64

T= 80 °C, P= 30 bar, t=3 h.

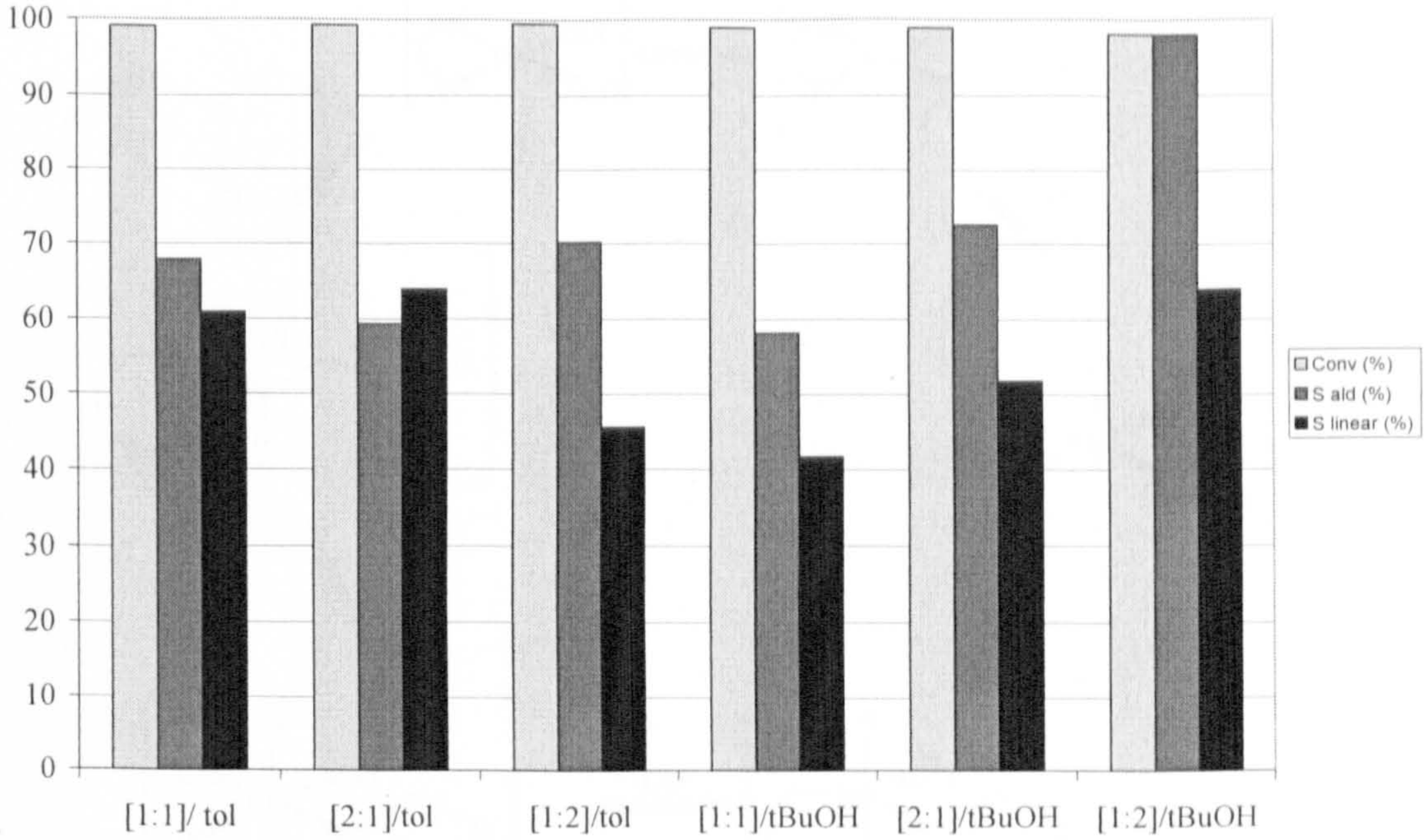


Figure 4- 16: Effect of CO: H_2 ratio on the hydroformylation of 1-octene catalysed by $[RhCl(CO)_2]_2$ and DTBPMB.

The total pressure, catalyst concentration, temperature and reaction time remained constant throughout and the CO:H_2 was varied from 1:2 to 2:1 in reactions carried out in two different solvents. We propose the mechanism showed in *Figure 4- 17* to operate when a source of chlorine is present in the reaction mixture. In toluene an increase in the partial pressure of CO (reduction of the partial pressure of H_2) leads to an increase in the selectivity to aldehydes and a decrease in the linear selectivity. This suggests that more of the branched alkyl intermediate undergoes migration onto CO under higher partial pressure of CO, thus leading to more aldehyde rather than isomerised alkene and lower linear selectivity.

The trend in ^{t}BuOH is different, with the highest CO partial pressure giving the best selectivity to aldehydes and the highest linear selectivity. The origin of this effect and why 1 to 1 CO to H_2 ratio gives the lower selectivity to aldehydes and lowest linear selectivity is not clear.

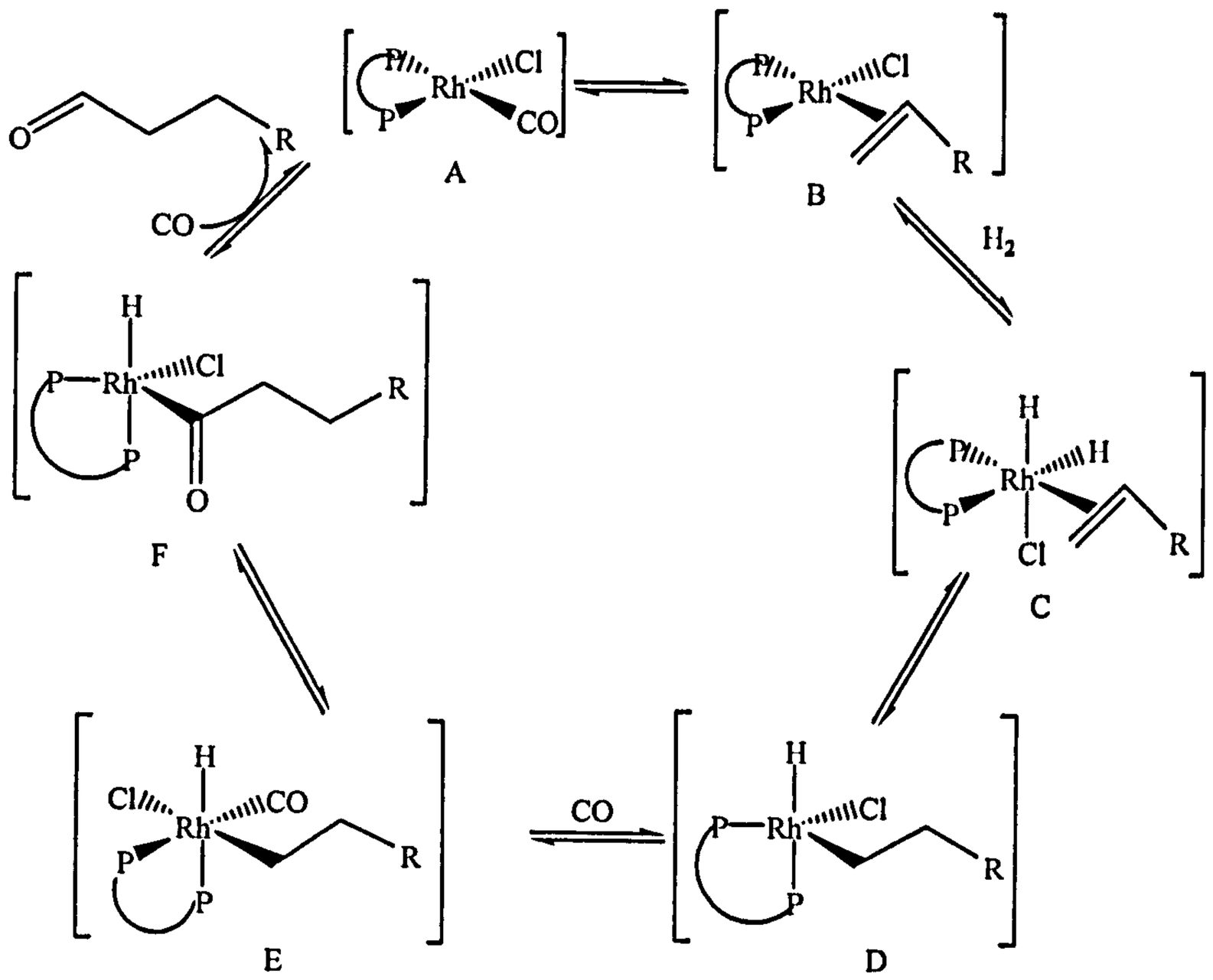


Figure 4- 17: Proposed mechanism operating in the hydroformylation with $[RhCl(CO)_2]_2$

4.2.2.2.4. Effect of the catalyst concentration.

In order to improve the conversion and the selectivity to aldehydes the rhodium and ligand concentration were increased from 3.83x 10^{-3} M to 7.66x 10^{-3} M, keeping the remaining reaction conditions unmodified, i.e., 30 bar and at 80 °C for 3 hours.

Figure 4- 18 shows the results obtained using two different catalyst concentrations. As previously mentioned, a high rhodium concentration leads to high rates and high l:b ratios, whereas a high ligand concentration leads to low rates and high l:b ratios. An improvement in selectivity to aldehydes and in selectivity to linear aldehyde was achieved when a higher rhodium and ligand concentration were used.

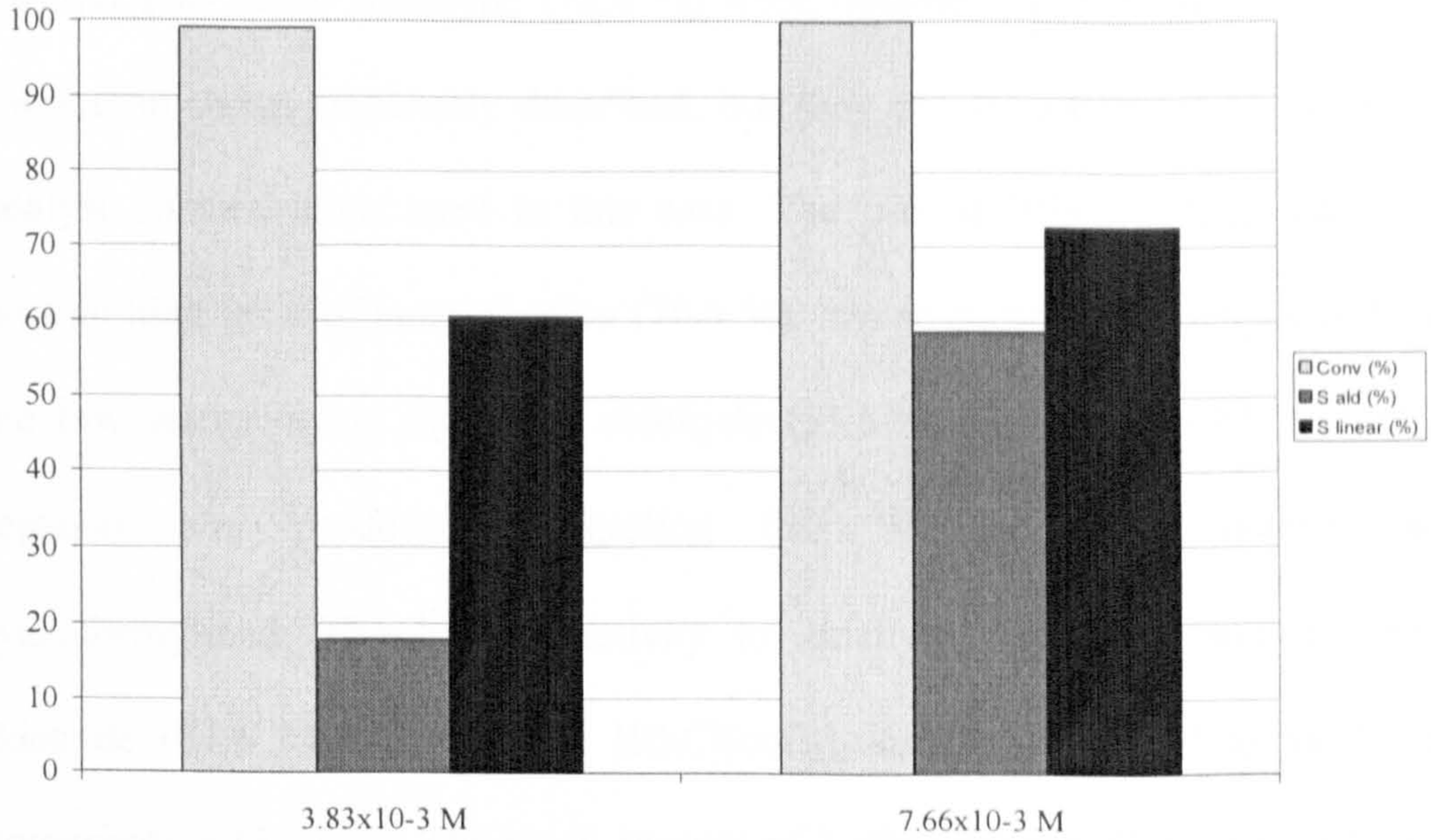


Figure 4- 18: Effect of catalyst concentration on the hydroformylation of 1-octene catalysed by $[RhCl(CO)_2]_2$ and DTBPMB.

4.2.2.3. $[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ as catalytic precursor.

$[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ were examined as chlorinated rhodium precursors for the hydroformylation of 1-octene.

Since both cyclooctene or cyclooctadiene are two labile very structurally similar groups, the active catalytic species were expected to be the same and afford the same products in similar yields (Table 4- 11)

Table 4- 11: Other chlorinated rhodium precursors

Rh precursor	[Rh](M)	[L](M)	Solv	Conv (%)	S ald (%)	S linear (%)
$[RhCl(cot)_2]_2$	2.4×10^{-3}	3.0×10^{-3}	Tol	86	51.3	81.6
$[RhCl(cod)_2]_2$	2.4×10^{-3}	3.0×10^{-3}	Tol	83.3	6.9	55.3
$[RhCl(CO)_2]_2$	2.4×10^{-3}	3.0×10^{-3}	Tol	58.1	50	78.6

T= 80 °C, P= 30 bar, t=3 h.

However, the conversion, selectivity to aldehydes and selectivity to nonanal observed in all cases were very different. When $[RhCl(CO)_2]_2$ was the catalytic precursor, 58.1 % conversion, low selectivity to aldehydes (50 %) and high

selectivity to linear aldehyde (78.6 %) were obtained. These values are much lower than those previously described, but they can be attributed to the lower catalyst concentration used in this case. The use of $[RhCl(cod)_2]_2$ led to an unusual high level of isomerisation (76.4 %), low selectivity to aldehyde (6.9 %) and low selectivity to the linear aldehyde (55.6 %). In this case 17 % 2-ethyl heptanal was produced, suggesting that the isomerised octenes are hydroformylated. The high selectivity to aldehyde (51.3 %), and to linear aldehyde (81.6 %) observed for $[RhCl(cot)_2]_2$ can be attributed to the lower isomerisation (33.7 %). The small amount of 2-ethyl hexanal (1 %) suggests that the internal alkenes are not trapped by CO. Thus, despite being structurally similar it seems that the active species formed from $[RhCl(CO)_2]_2$, $[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ are different.

4.2.2.3.1. Effect of the addition of base.

The hydroformylation reaction of 1-octene using $[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ was carried out in the presence of 0.14 mmol of the weak base, NEt_3. Not only did the selectivity to aldehydes improve but also alcohols were produced (Table 4- 12). Unfortunately, the selectivity to linear aldehyde decreased dramatically. These alcohols may be direct products of the hydroformylation reaction or they may arise from the hydrogenation of the aldehydes formed and therefore that aldehydes are involved in the catalytic cycle.

A similar effect on conversion to aldehyde and selectivity to linear aldehyde to those observed for $[RhCl(CO)_2]_2$ was observed for these two compounds. In the case of $[RhCl(cod)_2]_2$, an increase of the conversion from 83.3 % to 99.8 % was accompanied by a dramatic increase of the selectivity to aldehydes from 6.9 % to

51.8 %, whereas the selectivity to linear aldehyde remained unaffected. In addition, alcohols were produced in a 6 % yield, of which 56 % was 1-nonanol. For $[RhCl(cot)_2]_2$, the conversion increased from 86 % to 99.9 % with a selectivity to aldehydes of 74 %, of which 41.4 % were linear. Alcohols were found in 9.3 %, with a selectivity to 1-nonanol of 72 %.

Table 4- 12: Effect of addition of base

Rh precursor	[Rh](M)	[L](M)	Solv	Conv (%)	S ald (%)	S linear (%)
$[RhCl(cot)_2]_2$	$2.4x10^{-3}$	$3.0x10^{-3}$	Tol	99.9	74	41.4
$[RhCl(cod)_2]_2$	$2.4x10^{-3}$	$3.0x10^{-3}$	Tol	99.8	51.8	56.5

T= 80 °C, P= 30 bar, t=3 h.

4.2.2.4. [$RhCl_3 \cdot 3H_2O$] as catalytic precursor.

The hydroformylation of 1-octene was carried out using [$RhCl_3 \cdot 3H_2O$] as the rhodium precursor. The typical reaction conditions of temperature, pressure and catalyst concentration were employed ([Rh]= [DTBPMB]= $3.83x10^{-3}$M, P= 30 bar, T= 80 °C, t= 3h). MeOH was used as the solvent, and therefore acetal formation was expected. However, in order to avoid it, NaOAc was added in a stoichiometric amount, since acetal formation is also base catalysed. Unfortunately, not only were aldehydes produced in lower yield (8.3 %) but also the formation of acetals was promoted. In addition, despite the low selectivity to aldehydes the selectivity to the linear aldehyde was only 66 %.

4.2.2.5. [$Rh_2(OAc)_4$]as catalytic precursor.

The hydroformylation reaction of 1-octene catalysed by this rhodium precursor was carried out in DCM, so that chlorine would be present. Aldehydes were produced in a 54 % yield in a complete reaction after 3 hours. The selectivity

towards linear aldehyde was only 37 %, which may be due to the high isomerisation observed (45.2 %). In a separated experiment NaOAc was added stoichiometrically in order to neutralise the acetic acid that might be formed. Complete conversion occurred after 3 hours, producing only aldehydes, although the selectivity towards linear aldehyde was only 46 %.

4.2.2.6. Other structurally related ligands.

DIBMPB, DCypPMB and DPhPMB were tested in the hydroformylation of 1-octene. Both isobutyl and cyclopentyl groups have a secondary carbon attached to the phosphorus atom, and therefore the steric bulk around the metal will not be as high as that created by a tertiary carbon atom. DPhPMB is less bulky than DTBPMB. In addition, due to the electronic resonance in the ring, the phenyl groups create a moderately electron withdrawing ligand. As discussed in section 2.2.4, according to Tolman's cone angle the steric bulk of the analogous monophosphines is: $^{i}Bu_3P<Ph_3P<^{i}Pr_3P<Cy_3P<^{t}Bu_3P$[28] suggesting that the steric bulk of these bidentate phosphines would be: DIBPMB<DPhPMB<DCypPMB<DTBPMB.

In terms of their electron donating properties, the order would be: DPhPMB<DIBPMB<DCypPMB<DTBPMB. It has been established that highly basic diphosphines lead to slow catalysts and also to low l:b ratios. Decreasing the basicity of the phosphine the back donation from the metal centre to the CO is decreased, making its dissociation easy and also facilitating the coordination of the alkene. The electronic properties also affect the H migration. A highly basic diphosphine weakens the Rh-H bond making the H more hydridic and facilitating the its migration onto the coordinated alkene. Thus, the more hydridic this H is,

the more favoured the migration to the terminal position of the alkene will be, leading therefore to the branched Rh-alkyl intermediate.

4.2.2.6.1. [Rh(acac)(CO)$_2$] as the rhodium precursor.

In an attempt to obtain high conversion of 1-octene to nonanal three analogous of DTBPMB were used as ligands, isobutyl, phenyl and cyclopentyl using [Rh(acac)(CO)$_2$]. The results of the hydroformylation of 1-octene with these ligands are shown in Table 4- 13.

Table 4- 13: Effect of the ligand in the hydroformylation of 1-octene

Ligand	[Rh] (M)	[L] (M)	Solvent	Conv (%)	S ald (%)	S linear (%)
DTBPMB	3.83×10^{-3}	3.83×10^{-3}	Toluene	99.8	92.4	48.3
DTBPMB	3.83×10^{-3}	3.83×10^{-3}	DCM	98.4	28.8	82.3
DIBPMB	3.83×10^{-3}	3.83×10^{-3}	Toluene	98.1	93.6	64.3
DIBPMB	3.83×10^{-3}	3.83×10^{-3}	DCM	29.5	16.6	79.6
DPhPMB	3.83×10^{-3}	3.83×10^{-3}	Toluene	98	62.3	68.9
DPhPMB	3.83×10^{-3}	3.83×10^{-3}	DCM	71.5	77.1	83.5
DCypPMB	3.83×10^{-3}	3.83×10^{-3}	Toluene	100	56.7	93.6
DCypPMB	3.83×10^{-3}	3.83×10^{-3}	DCM	99.6	94	53.5

T= 80 °C, P= 30 bar, t=3 h.

All of them seem to be very good isomerisation catalysts under these conditions, giving low selectivity to aldehydes, which is consistent with the previous findings. Traditionally, high l: b ratios are observed for less negatively charged metal centres (formed with electron withdrawing phosphines), which are presumed to favour the formation of 1-alkylrhodium complexes.[15] An increase on the congestion around the metal is produced by enlarging the bulk of the substituents on the phosphorus atom. This favours the less sterically demanding transition state, forcing the reaction to go towards the formation of the linear aldehyde. According to the steric properties, DTBPMB is expected to give the

highest linear selectivity. Considering the electronic properties, H migration to form a 1-alkylrhodium intermediate will be enhanced by a more electrophilic rhodium centre, which will be provide by a poor electron donating ligand. DPhPMB is the least electron donating of the three new ligands and therefore it should lead to the highest linear selectivity.

4.2.2.6.2. $[RhCl(CO)_2]_2$ as the rhodium precursor.

DCypPMB and DPhPMB were also used as the ligands to modify $[RhCl(CO)_2]_2$ as rhodium precursor. The results obtained are shown in Table 4- 14 and *Figure 4- 19*.

Table 4- 14: Effect of the ligand

Ligand	[Rh](M)	[L] (M)	Solv	Conv (%)	S ald (%)	S linear (%)
DTBPMB	$3.83x10^{-3}$	$3.83x10^{-3}$	DCM	97.3	70.6	63.1
DPhPMB	$3.83x10^{-3}$	$3.83x10^{-3}$	DCM	99.5	49	71.0
DCypPMB	$3.83x10^{-3}$	$3.83x10^{-3}$	DCM	96.3	12	63.3

T= 80 °C, P= 30 bar, t=3 h.

None of these ligands combined with $[RhCl(CO)_2]_2$ improved the conversion, the selectivity to aldehydes or the selectivity to linear aldehyde achieved with the system $[RhCl(CO)_2]_2$/DTBPMB. Considering the low selectivity to aldehydes achieved after 3 hours, it seems that the less bulky and less electron donating ligands are better isomerisation catalysts than the one derived from DTBPMB. A high isomerisation of 1-octene (very little 1-octene available for hydroformylation) is reflected in the low conversion to aldehydes, the low selectivity to the linear aldehyde and the presence of 2-ethyl heptanal in all cases.

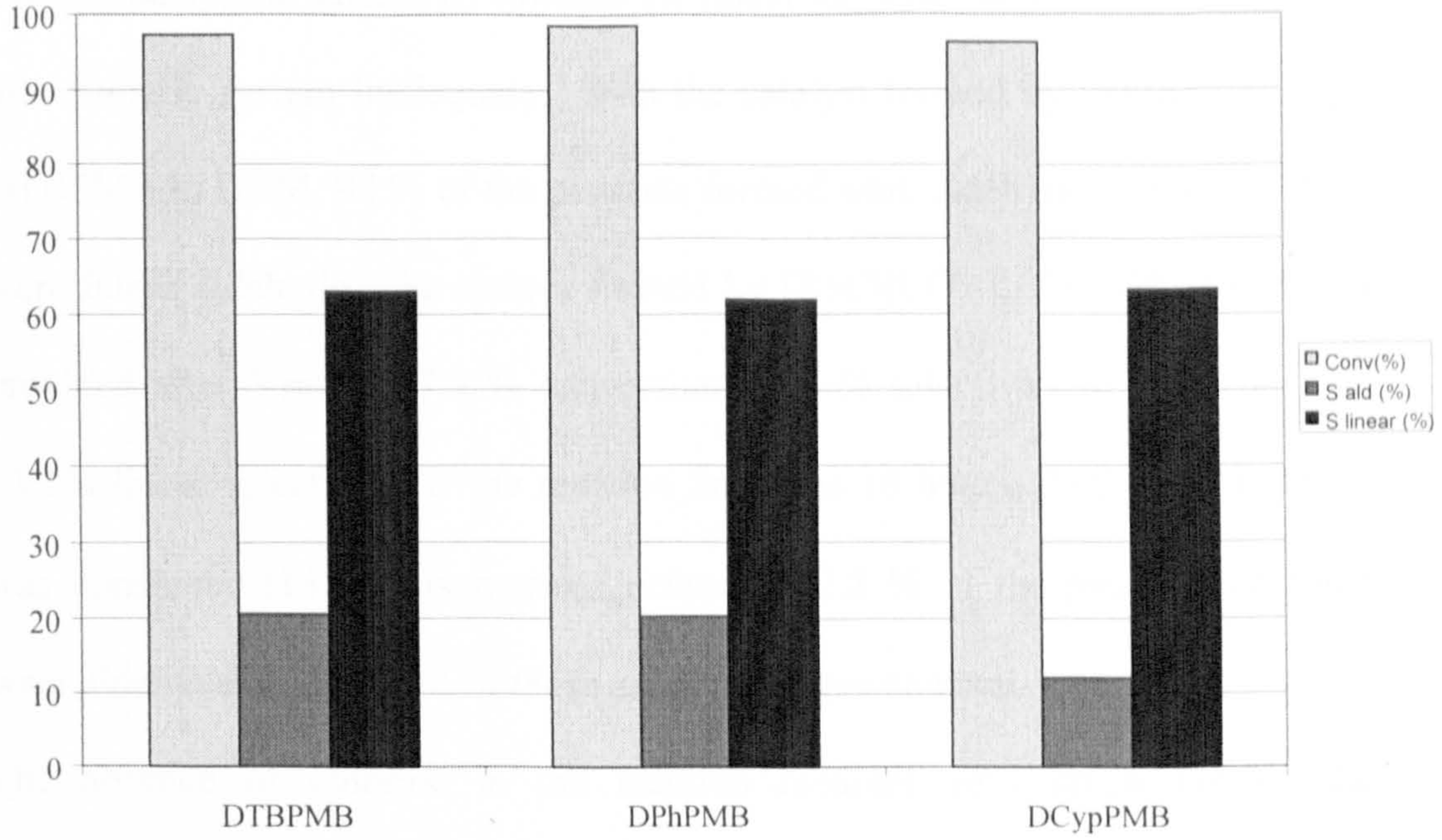


Figure 4- 19: Effect of different ligands on the hydroformylation of 1-octene catalysed by $[RhCl(CO)_2]_2$.

4.2.2.7. Comparison of rhodium precursors.

In order to have a general view of the effectiveness of each rhodium precursors *Figure 4-21* shows the most satisfactory results obtained with each of them.

$[RhCl(cod)_2]_2$ turned out to be the least effective of the rhodium precursors, giving only 83.3 % conversion 6.9 % selectivity to aldehydes and 55.3 % selectivity to linear aldehyde. The use of $[RhCl(cot)_2]_2$ improved greatly upon the results obtained with the structurally similar $[RhCl(cod)_2]_2$ (86 % conversion, 51.3 % selectivity to aldehydes and 81.6 % selectivity to linear aldehyde). When using either $[Rh(acac)(CO)_2]$ or $[Rh_2(OAc)_4]$ the reaction went to completion after 3 hours. $[RhCl(CO)_2]_2$ was also very active, giving nearly complete conversion after 3 hours. In terms of aldehyde formation, $[Rh_2(OAc)_4]$ turned out to be the best, since the only aldehydes were observed at end of the reaction.

Unfortunately, the selectivity towards the linear aldehyde was only 46 %, making this catalytic system inadequate. With the catalyst formed by [Rh(acac)$(CO)_2$]/ DTBPMB in DCM, 94 % of the products formed were aldehydes, of which 59 % were linear aldehyde. The system formed by [RhCl$(CO)_2]_2$/ DTBPMB in DCM provided after 3 hours 97.3 % conversion, 70.6 % selectivity to aldehydes and 63.1% linear selectivity. If the reaction time was 18 hours, 99.5 % of 1-octene was consumed (16.7 % isomerised octenes), 82.8 % of the products obtained were aldehydes and 76.3 % of these aldehydes were nonanal.

The absence of chlorine in the reaction medium very much favours the production of aldehydes. However, very low selectivity to linear aldehyde was observed, suggesting that 1-octene was isomerised to internal octenes and these were hydroformylated, leading to branched aldehydes. The presence of chlorine in the reaction medium does not inhibit the isomerisation but it partially inhibits the hydroformylation of internal alkenes, leading to higher selectivity to linear products but lower aldehyde selectivity.

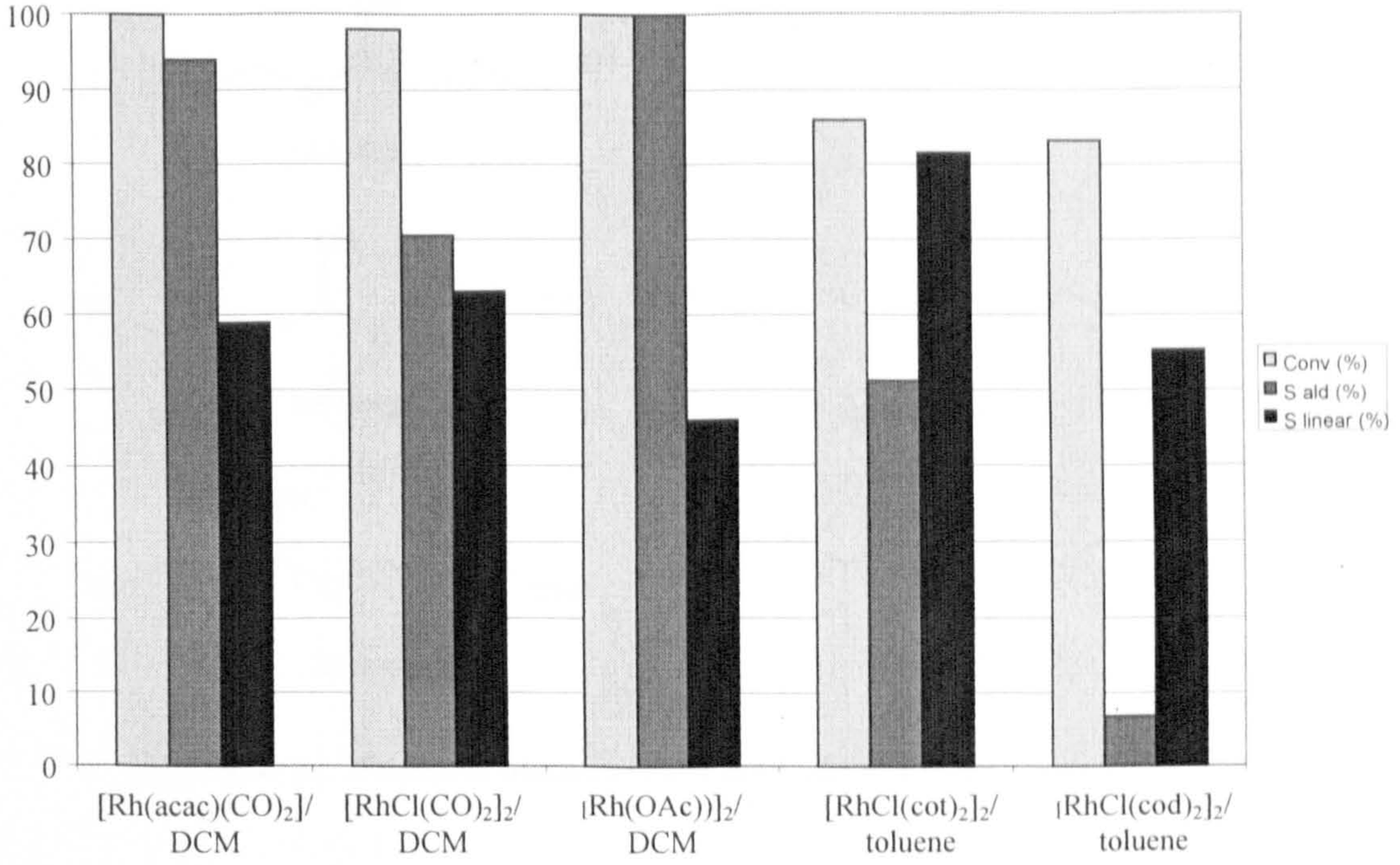


Figure 4- 20: Comparison of different rhodium precursors.

4.2.3. Hydroformylation of allyl alcohol.

Allyl alcohol is a very interesting substrate, since the direct formation of alcohols produces 1, 4-butanediol. The main use of this diol is as a precursor for the production of other essential chemicals, such as THF, polybutylene terephthalate resins or γ-butyrolactone. Being such an interesting substrate, the selective production of either 4-hydroxybutanal or 1,4-butanediol was investigated. As for the two previous substrates, a study of different rhodium precursors was carried out, since not all of them gave the same values of conversion and selectivity.

The linear aldehyde product, (4-hydroxybutanal, HB), undergoes internal condensation to form 2-hydroxyfuranol (HF), the branched aldehyde is 3-hydroxy-2-methylpropanal (HMP). The rest of the products observed arises from the aldol condensation of 4-hydroxybutanal, 3-hydroxy-2-methylpropanal and allyl alcohol (*Figure 4- 21*).

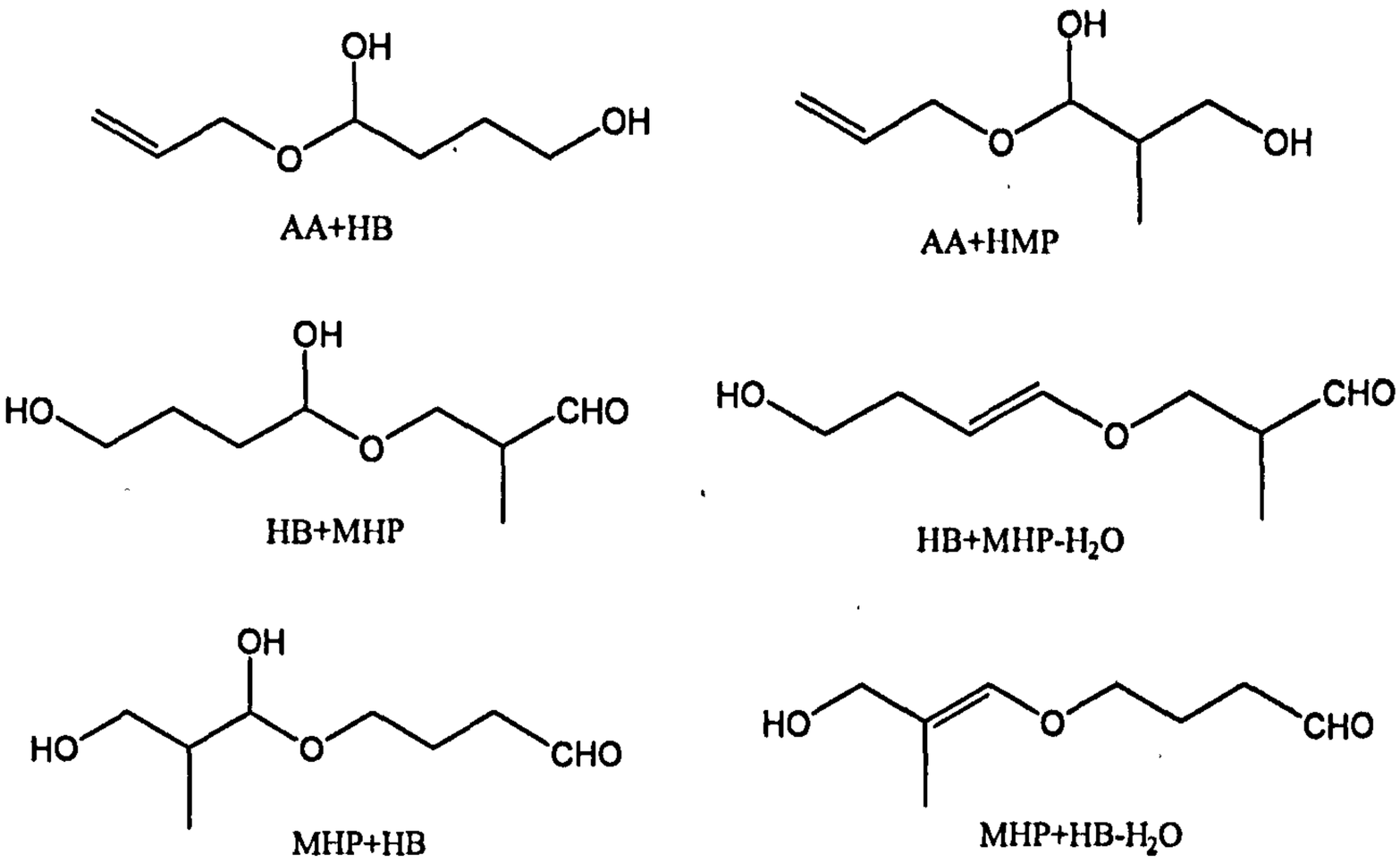


Figure 4- 21: Products obtained from allyl alcohol hydroformylation

4.2.3.1. $RhCl(CO)_2]_2$ as catalytic precursor.

The first attempt to hydroformylate allyl alcohol with $[RhCl(CO)_2]_2$ under the standard conditions ([Rh]=[DTBPMB]= 3.83 x 10^{-3} M, T= 80 °C, P= 30 bar, t= 3 h) led to the formation of aldol condensation products. Variations in the solvent, catalyst concentration, pressure and the rig were investigated. The results obtained are summarised in Table 4- 15.

4.2.3.1.1. Effect of the solvent.

Toluene and OctMiMTfN (entries 1 and 2) were the solvents studied. It was found that using toluene as the solvent only long aldol condensation products, HB+MHP (34 %), HB+MHP-H_2O (16.4 %), MHP+HB (40.5 %), MHP+HB-H_2O (9 %), were formed, whereas using OctMiMTfN as the solvent the two aldehydes expected from the direct hydroformylation of allyl alcohol were also formed (11.5 % HF, 10 % MHP), although in lower yield than that of aldol condensation products. Thus, as far as the solvent is concerned in this catalytic

system, a polar solvent favoured the formation of simple aldehydes over aldol condensation.

4.2.3.1.2. Effect of the pressure.

The reaction was carried out in toluene at 80 °C under 10, 30 and 60 bar of synthesis gas (entries 1, 3, 4). Using a rhodium concentration of $3.8x10^{-3}$ M and under 10 bar pressure no reaction took place and only traces of unknown products were detected by GC. At 30 bar only long aldol condensation products were obtained, HB+MHP (34 %), HB+MHP-H_2O (16.4 %), MHP+HB (40.5 %), MHP+HB-H_2O (9 %), whereas at 60 bar, although long aldol condensation products were still the major products, HB+MHP (42.9 %), HB+MHP-H_2O (8.6 %), MHP+HB (36.1 %), MHP+HB-H_2O (2 %), a small amount of the desired short aldehydes were observed (5.8 % HF, 2.6 % MHP).

At a rhodium concentration of $7.7x10^{-3}$ M and 10 bar pressure (entry 7), HB (27.9 %), HB+AA (41.9 %) and MHP (10.4 %) were produced. Under 30 bar of synthesis gas (entry 6) the two desired aldehydes were formed, the branched in higher proportion than the linear (6.7 % HF, 17.5 % MHP). However, HB+ AA was the major product (62.8 %). Under 60 bar of pressure (entry 8) the major products were again the aldol condensation products but small amounts of HF (6.1 %) and MHP (5.4 %) were also observed.

4.2.3.1.3. Effect of the catalyst concentration.

To influence the rate of the reaction, the concentration of rhodium and DTBPMB were doubled. A comparative study under different pressures was also carried out. The results obtained are shown in *Figure 4- 22* and *Figure 4-23*.

Not only does an increase of the catalyst concentration from 3.83×10^{-3} M to 7.66×10^{-3} M when the pressure is 30 bar produce a big decrease in the long aldol condensation products, but also the branched aldehyde, MHP, and the linear hemiacetal, HB+ AA are produced in high yield (entries 1 and 6). Surprinsingly, the linear aldehyde HB was not observed in any case, suggesting that the hemiacetal formation between HB and AA is faster than the internal hemiacetal formation to form HF.

When the pressure was increased to 60 bar (entries 4 and 8), the desired aldehydes were formed in low yield and the proportion of aldol condensation products remained almost unaffected. An increase in the catalyst concentration did not affect the selectivity to 2-hydroxy-furanol, but the selectivity towards the branched aldehyde increased.

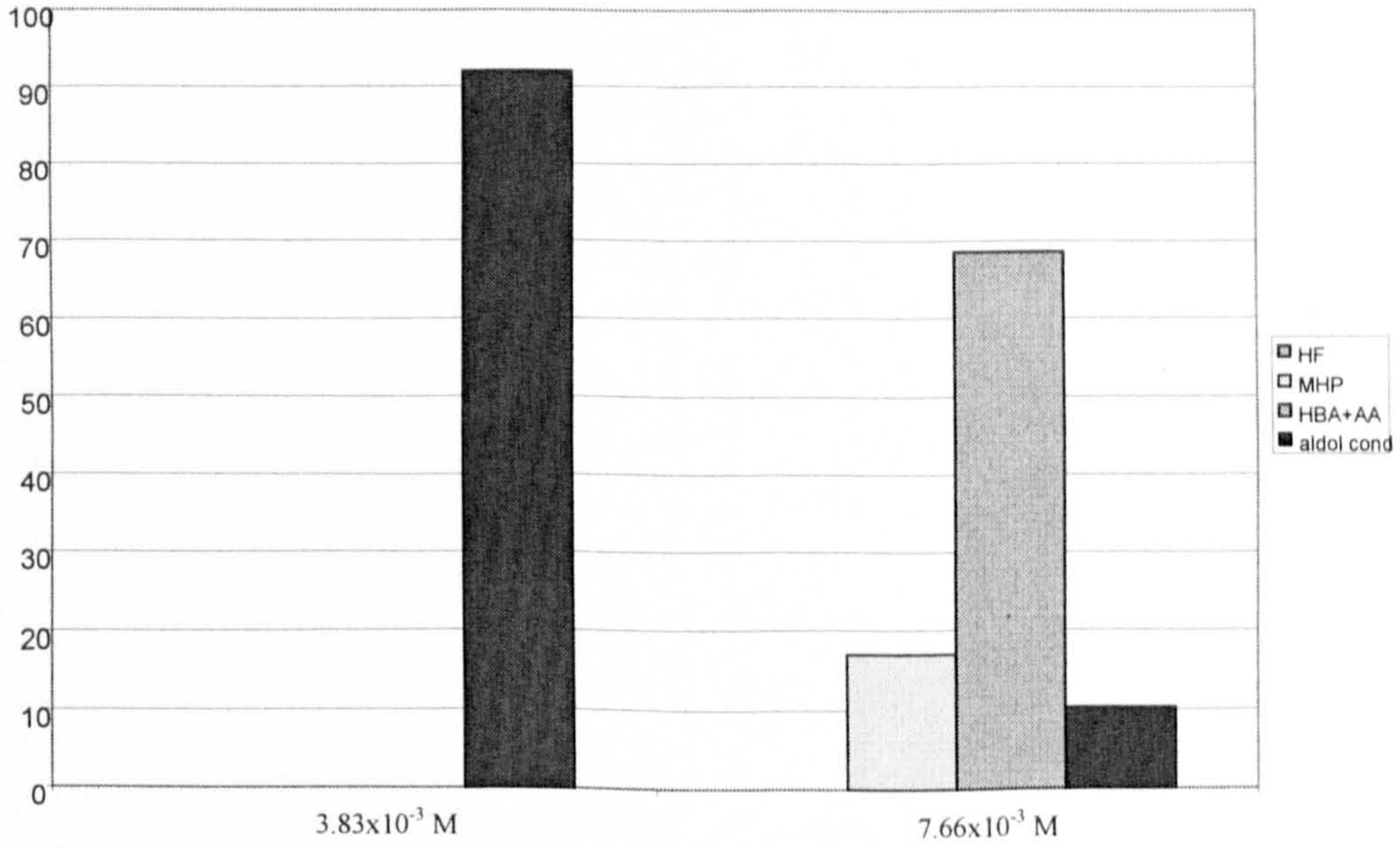


Figure 4- 22: Effect of the catalyst concentration on the hydroformylation of allyl alcohol catalysed by $[RhCl(CO)_2]_2$ and DTBPMB at 30 bar.

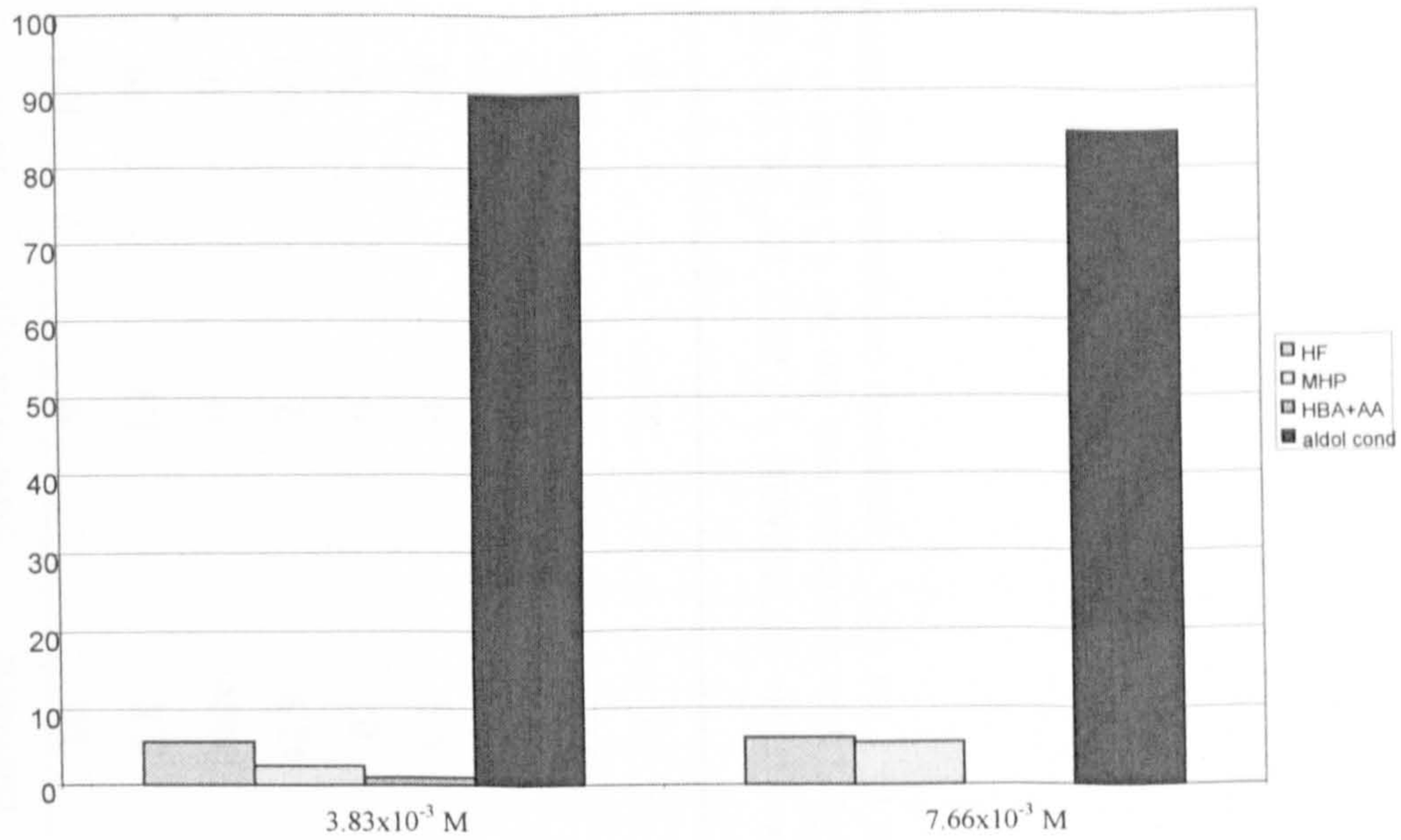


Figure 4- 23: Effect of thecatalyst concentration on the hydroformylation of allyl alcohol catalysed by $[RhCl(CO)_2]_2$ and DTBPMB at 60 bar.

Table 4- 15: Hydroformylation of allyl alcohol with $[RhCl(CO)_2]_2$.

Entry	P (bar)	HF	MHP	AA+HB	AA+MHP	HB+MHP-H_2O	HB+MHP	MHP+HB-H_2O	MHP+HB
$1^{(*)}$	30	0	0	0	0	16.4	34	9	40.5
$2_a^{(1,*)}$	30	11.5	10	0.7	7.6	0	5.8	1.3	89
$3_b^{(*)}$	10	0	0	0	0	Trace	Trace	0	0
$4^{(*)}$	60	5.8	2.6	1.6	0	8.6	42.9	2	36.1
$5^{(2,*)}$	30	0	15.4	0	76	0	0	0	0
$6^{(**)}$	30	6.7	17.5	0	62.8	0	5.5	0	4.8
$7_b^{(**)}$	10	27.9	10.4	1.8	41.9	1.2	4.1	0	7.4
$8^{(**)}$	60	6.1	5.4	1.5	0	6.3	49.3	2.1	26.9
$9_c^{(3,*)}$	30	0	17.0	0	68.6	0	0	0	5.6

All the experiments were run in toluene at 80°C for 3 hours. (*): [Rh]= [DTBPMB] = 3.83 x 10^{-3} M, (**):[Rh]= [DTBPMB] = 7.66 x 10^{-3} M, (1): This experiment was run in OctMiMTfN. (2): This experiment was run for 1 hour in a rig with better stirring (3): This experiment was run for 4.5 hours in a rig with better stirring. (a): 5 unknown compounds were present (24.8 %). (b) 2 unknown compounds present (5.3 %). (c): 1 unknown compound was present (3.3 %)

4.2.3.1.4. Effect of the rig.

Given the mixture of products and the different yields obtained in all cases, it was likely that the reason for this was a bad mixing between the solution and the gas. The mass transport seemed to be very poor, since no good selectivity to the desired products had been observed so far. Thus, in order to get a better mixture of the gas and the catalyst the reaction was run in another rig in which the stirring was better.

When the reaction was run in the new rig under the same conditions as the first experiment (entry 9), only two main products were observed, MHP (17 %) and MHP+ AA (68.6 %), whereas when poorly stirred autoclaves were used, the products formed come exclusively from aldol condensation (entry 1). Therefore, as suspected, the reaction appears to be very sensitive to mass transport effects.

4.2.3.2. $[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ as catalytic precursors.

$[RhCl(cot)_2]_2$ and $[RhCl(cod)_2]_2$ were also studied for the hydroformylation of allyl alcohol in toluene (entries 1-4 in Table 4- 16). Under the standard reaction conditions used ([Rh]=[DTBPMB]= 3.83×10^{-3} M, T= 80 °C, P= 30 bar, t= 3 h) both catalysts performed similarly, producing mainly aldol condensation products (> 65 %). The addition of NaOAc as a base had a dramatic effect, since the desired aldehydes were formed in > 80 % yield. Surprisingly, the presence of base promoted the formation of the desired products over the aldol condensation products.

4.2.3.3. $[Rh_2(OAc)_4]$ as catalytic precursor.

The effect of a base was investigated in the hydroformylation of allyl alcohol in toluene using $[Rh_2(OAc)_4]$ as the catalytic precursor (entries 5-8 in Table 4- 16) under the typical reaction conditions ([Rh]= [DTBPMB]= $3.83x10^{-3}$ M, T= 80 °C, P= 30 bar, t= 3 h). The reaction was carried out in the absence and in the presence of a base. The highest selectivity to the desired product (75.1 %) was obtained when NaOAc was added in a ratio of Rh: base= 1:3 (entry 6). In addition, the long aldol condensation products were formed in lower yield (<8 %). However, a higher amount of base led to a dramatic increase of these aldol condensation products (>75 %) and the desired products became minor (<10 %) (entry 7). The use of KO^tBu as base had the same effect (entry 8).

4.2.4. Vinyl acetate hydroformylation.

This substrate has not been studied as extensively as the previous three. Nevertheless, as a first approach, three hydroformylation reactions have been carried out, with $[Rh(acac)(CO)_2]$ in DCM, $[RhCl(CO)_2]_2$ in toluene and with $[Rh_2(OAc)_4]$in DCM.

The desired product was the branched aldehyde. Given the high selectivity towards linear products provided by this ligand, it was quite surprising to get 100 % of the branched product in a complete reaction after 3 hours. This high selectivity towards the branched product can only be explained considering electronic properties of vinyl acetate. When it coordinates the metal centre, the carbon bonded to the rhodium atom will have negative charge and the intermediate able to stabilise it, will be favoured. It is logical to think that the

carbon closer to the oxygen atom will accept the negative electron density better than the further one, favouring then the formation of the branched aldehyde.

4.2.5. Conclusions.

In this chapter we have carried out a detailed study of hydroformylation reactions of terminal alkenes and allyl alcohol together with preliminary studies on vinyl acetate. This study has been focused on the catalytic activity of different rhodium complexes modified by different ligands and on the different species formed between them which may be involved in the catalytic cycle.

For the hydroformylation of 1-hexene, $[RhCl(CO)_2]_2$, $[Rh(acac)(CO)_2]$, $[Rh(OAc)_2]_2$ and $[RhCl_3{\cdot}3H_2O]$ were used as the rhodium precursors and for the hydroformylation of 1-octene $[RhCl(cod)_2]_2$ and $[RhCl(cot)_2]_2$ were used in addition to those previously mentioned. High conversions and selectivities were achieved by having chlorine present in the solution, either in the solvent (DCM) or by using a chlorine containing rhodium precursor.

The influence of the ligand on the catalyst productivity has been investigated. Some ligands structurally related to DTBMPB, such as DIBPMB, DPhPMB and DCypPMB, were the target of this study. The most satisfactory results were achieved when DTBPMB was used as the ligand, as for the methoxycarbonylation of alkenes.

Table 4- 16: Hydroformylation of allyl alcohol with $[RhCl(cot)_2]_2$, $[RhCl(cod)_2]_2$ and $[Rh_2(OAc)_4]$

Rh precursor	Entry	Conv (%)	HF	MHP	AA+HBA	HBA+AA-H_2O	HBA+AA	MHP+AA-H_2O	MHP+AA
$[RhCl(cot)_2]_2$	1_a	93	12	2	6.66	5.8	14.8	9.9	35.4
	$2^{(1)}$	86	65.9	17.7	0	0	0	0	0.5
$[RhCl(cod)_2]_2$	3	98.5	13.9	5.8	4.1	17.2	40.4	9.3	21.1
	$4^{(2)}$	86.6	73.8	12.9	0	0	0	0	0
$[Rh_2(OAc)_4]$	5	94.5	7.3	11.1	33.7	18.6	12.9	0.5	10.4
	$6^{(2)}$	100	75.1	17	0.3	0.7	4	0.8	2.1
	$7^{(3)}$	98.6	5.7	2.7	12.1	5.4	32	6.9	33.8
	$8^{(4)}$	98.9	12	3.6	2.7	16	19.1	5.2	40.3

All the experiments were run in toluene at 80 °C and 30 bar for 3 hours. [Rh]= [DTBPMB]= $3.83x10^{-3}$ M. (1): This experiment was carried out in the presence of 0.07 mmols of NaOAc. 2.2 % unknown compounds. (a): 6.7 % unknown compounds. (2): This experiment was carried out in the presence of 0.07 mmols of NaOAc. (3): This experiment was carried out in the presence of 0.12 mmols of NaOAc. (4): This experiment was carried out in the presence of 0.02 mmols of K^{t}BuO

4.2.6. References.

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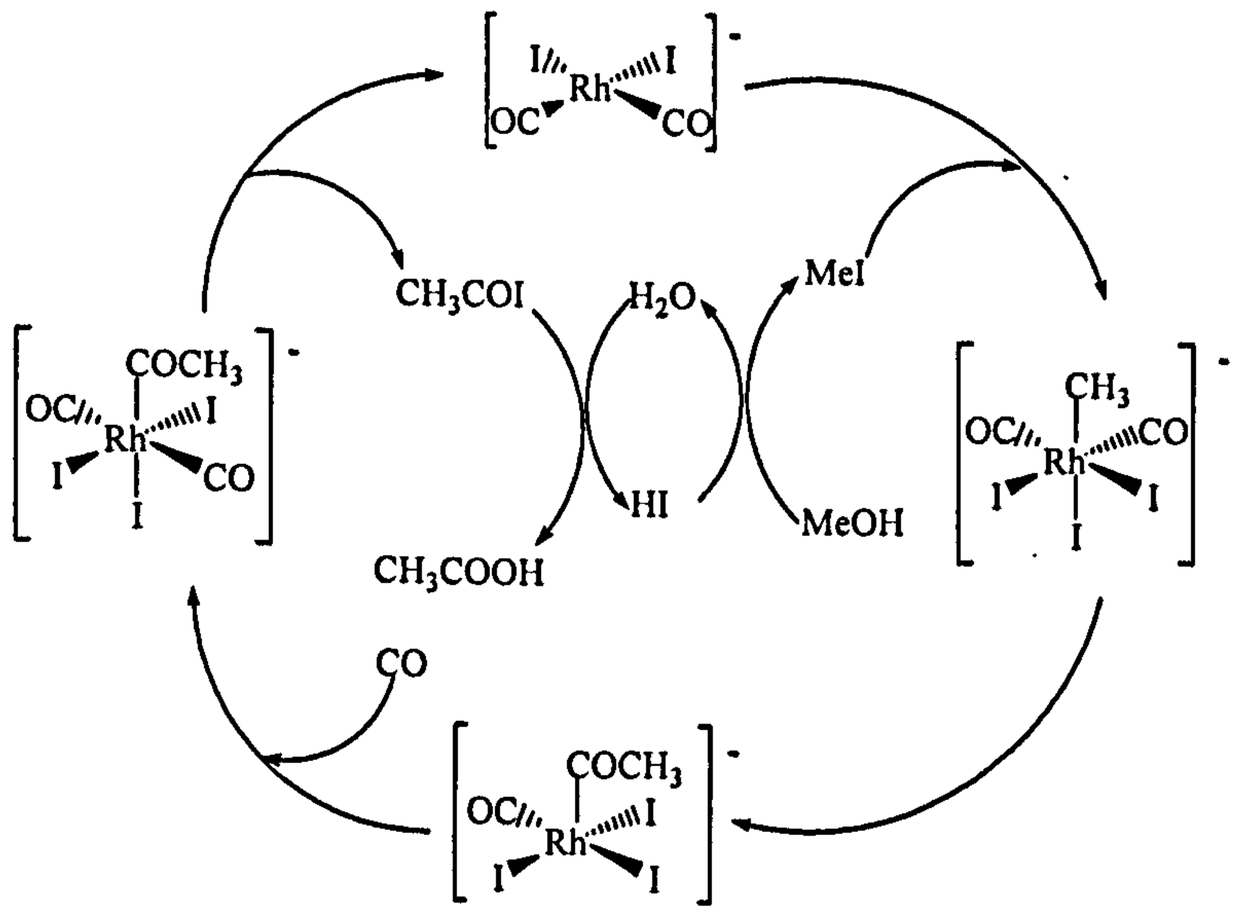
Chapter 5:

METHANOL CARBONYLATION

5.1. Methanol carbonylation

Acetic acid is an important chemical used for a wide range of processes. More than 5.5 million tonnes are produced per year.[1] The rhodium based catalysed carbonylation of methanol to acetic acid was first commercialised by Monsanto in 1960s[2] replacing the BASF cobalt-catalysed process.[3,4] The Monsanto catalytic system is effective in a pressure range of 30-60 atm between 150-200 °C using a rhodium concentration of 0.001 M in a variety of solvents, a mixture of acetic acid and methyl acetate being preferred.[1,5] The mechanism operating in the Monsanto process is shown in *Scheme 5- 1*.



Scheme 5- 1: Rhodium catalysed methanol carbonylation

The catalytic cycle starts with $[Rh(CO)_2I_2]^-$, which is the active species. At room temperature in the presence of methyl iodide oxidative addition occurs to lead to the rhodium (III) hexacoordinate intermediate $[Rh(CO)_2I_3Me]^-$. Fast migratory insertion of CO onto the Rh-CH_3 bond affords a pentacoordinate intermediate $[Rh(COMe)(CO)I_3]^-$, which easily coordinates CO to form the hexacoordinate intermediate $[Rh(COCH_3)(CO)_2I_3]^-$. This species reductively eliminates MeCOI regenerating the initial rhodium species.

In the Monsanto process the reaction is first order in rhodium and methyl iodide and zero order in methanol and CO partial pressure, showing that the rate determining step is oxidative addition of methyl iodide to $[RhI_2(CO)_2]^-$.[3,7] An enhancement on the rate and the catalyst stability by the addition of water has been reported.[8,9]

The major energy cost of the process under Monsanto conditions is the separation of water (>15 % w/w) from acetic acid. An alternative process at lower water concentration was developed by Hoechst Celanese. Using the low water concentration comparable rates were achieved. Water hydrolyses acetyl iodide to form acetic acid, reduces $[Rh(CO)_2I_4]^-$, which constitute the decomposition pathway of the catalyst, to $[Rh(CO)_2I_2]^-$ and increases the rate of oxidative addition.[11] The incorporation of an inorganic or organic halide has a promoting effect in addition to avoiding the formation of RhI_3, which is an insoluble catalyst decomposition product. At high iodide the concentration of methyl iodide increases because of the reaction shown in *Scheme 5- 2* and therefore higher rates are achieved since the reaction is first order in [MeI].

$$MeOAc + I^- \rightleftharpoons MeI + OAc^-$$

Scheme 5- 2: Formation of methyl iodide from methyl acetate and inorganic iodide

By increasing the concentration of methyl acetate, the water gas shift reaction (WGSR) is also inhibited because HI is scavenged by the reaction shown in *Scheme 5- 3*.

$$HI + MeOAc \longrightarrow MeI + HOAc$$

Scheme 5- 3: Scavenging of HI by MeOAc

The WGSR is a side reaction, the first step of which (reaction 1 in *Scheme 5- 4*) constitutes the main catalyst decomposition pathway. The active species is also involved in this reaction (*Scheme 5- 4*).

$$[Rh(CO)_2I_2]^- + 2\,HI \longrightarrow [Rh(CO)_2I_4]^- + H_2 \quad (1)$$

$$[Rh(CO)_2I_4]^- + H_2O + CO \longrightarrow [Rh(CO)_2I_2]^- + 2\,HI + CO_2 \quad (2)$$

$$H_2O + CO \longrightarrow H_2 + CO_2 \quad (3)$$

Scheme 5- 4: The water gas shift reaction catalysed by $[RhI_2(CO)_2]^-$

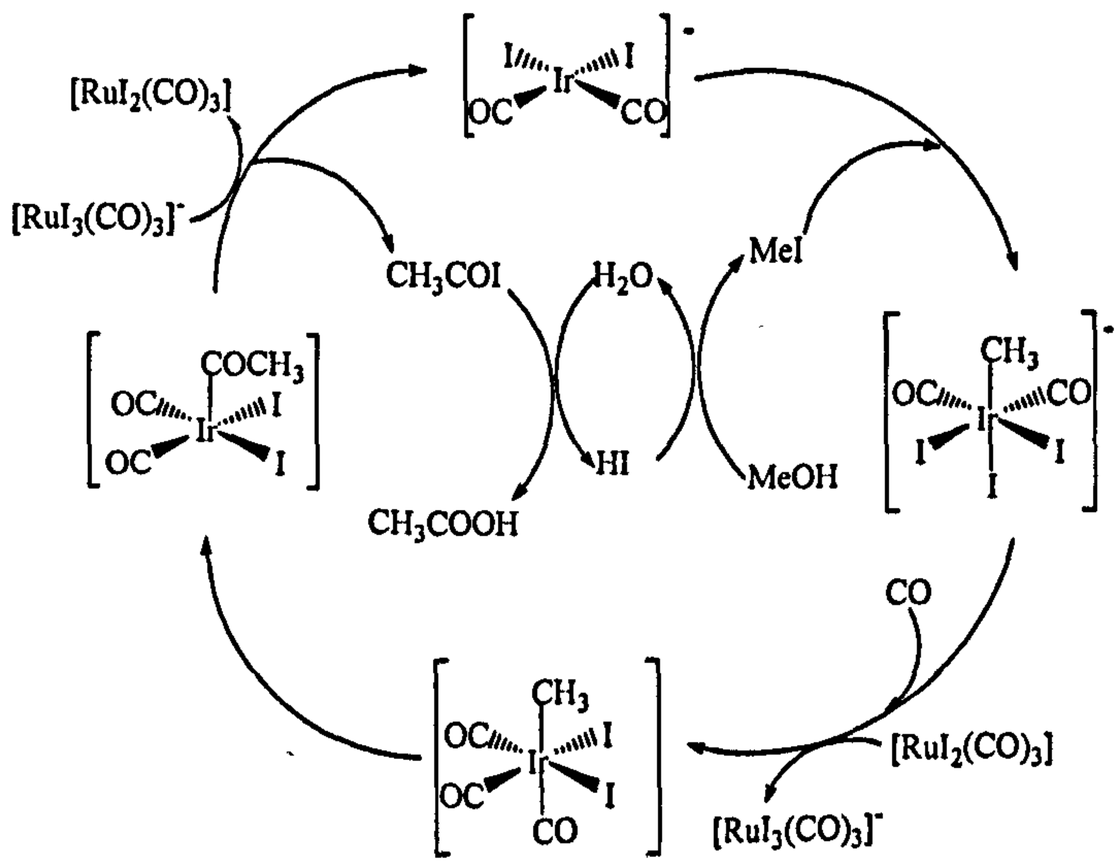
The conversion of $[Rh(CO)_2I_2]^-$ to $[Rh(CO)_2I_4]^-$ leads to a reduction in the concentration of the active rhodium species and therefore to a reduction in the carbonylation rate. In addition, $[Rh(CO)_2I_4]^-$ is susceptible to loss of CO leading to RhI_3.[8] A high concentration of water and a low concentration of HI reduces the rate of oxidation of $[Rh(CO)_2I_2]^-$ preventing the formation of solid RhI_3. However, HI is necessary in the reaction mixture to produce methyl iodide from methanol and methyl acetate. Water also drives reaction 2 in *Scheme 5- 4*, which regenerates the active catalyst.

The concentration of methyl acetate affects the concentration of HI changing the rate determining step of the WGSR. At low HI concentration, the oxidation is likely to be the rate determining step since the concentration of the active species is high. The higher concentration of iodide promotes the formation of a strong nucleophile five-coordinate dianionic intermediate $[RhI_3(CO)_2]^{2-}$ which is highly active towards oxidative addition of methyl iodide.[11,12] Unfortunately this intermediate has not been detected spectroscopically since its concentration is much lower than the monoanionic species.

Since oxidative addition of methyl iodide to the rhodium (I) active species $[Rh(CO)_2I_2]^-$ determines the rate of the reaction, the addition of electron donating

phosphines should accelerate the process. Previous work by Cole-Hamilton and coworkers showed that the use of triethyl phosphine rhodium complexes as the catalyst for this reaction leads to higher activity than that obtained with the unmodified rhodium active complex under industrial conditions, but the catalyst was unstable to phosphine loss.[5]

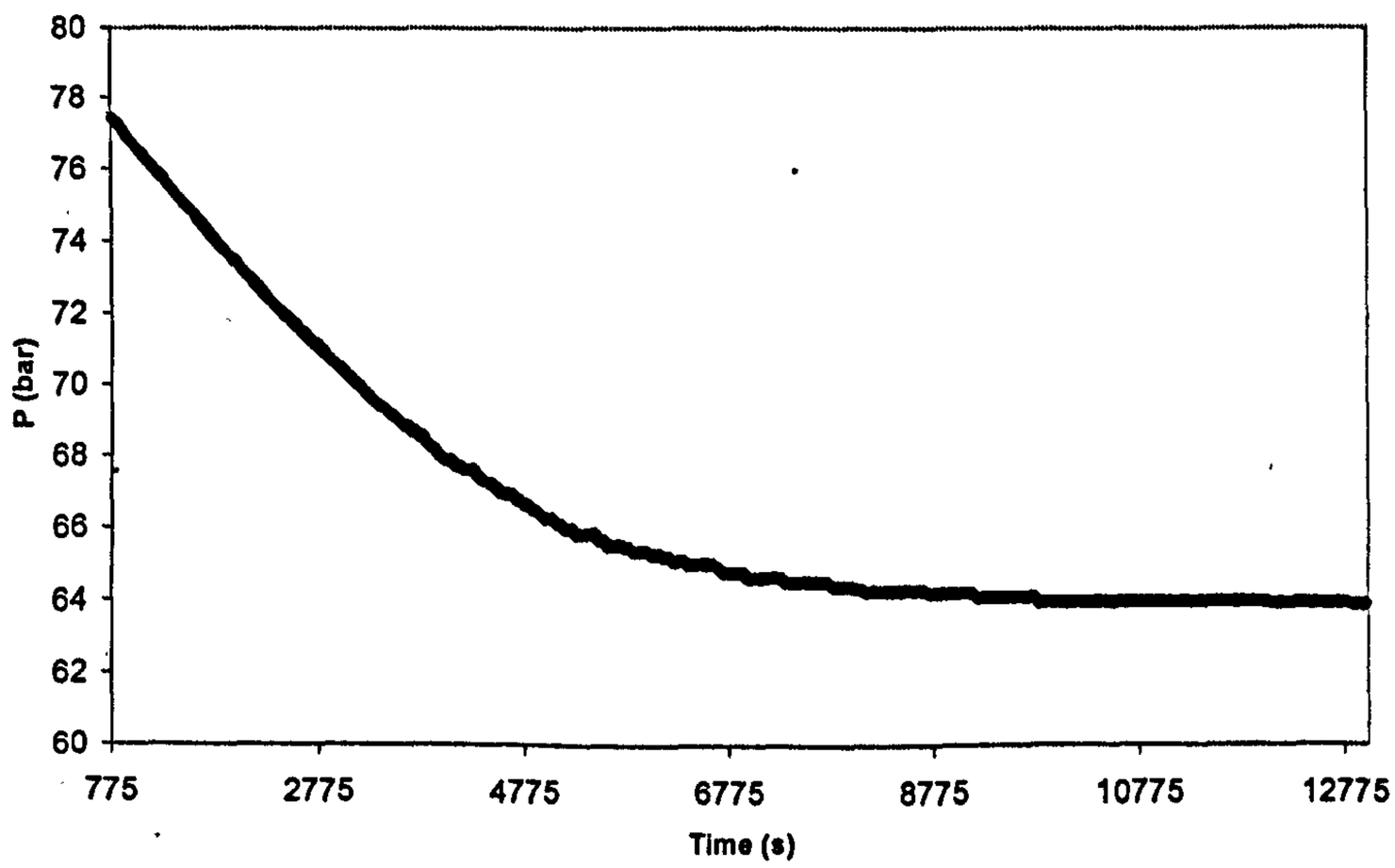
In 1996 BP Chemicals commercialised the iridium-catalysed methanol carbonylation.[6] The catalyst used in this process is based in an iridium precursor, methyl iodide and a ruthenium promoter. This process operates under milder conditions of pressure and temperature than the Monsanto process. The lower concentration of water reduces the cost considerably compared with that of the Monsanto process. The proposed mechanism is shown in *Scheme 5- 5*. The cycle starts with $[Ir(CO)_2I_2]^-$. Rapid oxidative addition of methyl iodide generates $[Ir(Me)(CO)_2I_3]^-$. Replacement of iodide (assisted by the Ru promoter) by CO increases the electron density on the metal centre weakening the Ir-CO bond and therefore facilitating the migration of methyl into the Ir-CO bond to form $[Ir(COMe)(CO)_2I_2]$, which recoordinates iodide to form $[Ir(COMe)(CO)_2I_3]^-$. Reductive elimination of MeCOI regenerates the initial species.



Scheme 5- 5: Iridium catalysed methanol carbonylation

5.2. Catalysis using Rh-DTBPMB complexes performed at constant pressure

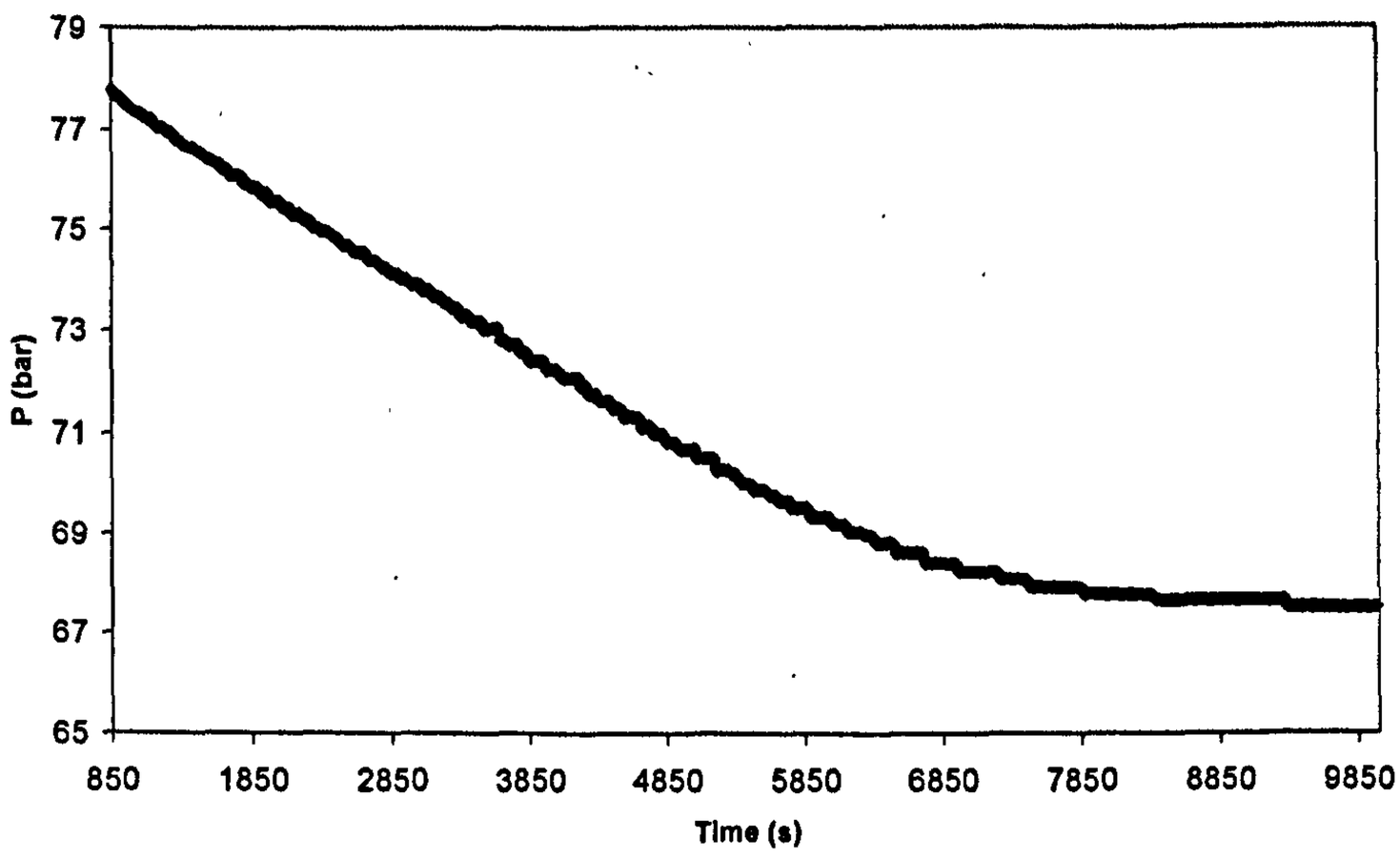
The catalytic system based on $[RhCl(CO)_2]_2$ and DTBPMB was tested using acetic acid conditions (MeOAc/HOAc/H_2O/MeI) at 150 °C under 27 bar of CO and 17 % w/w of H_2O. Under these conditions a slightly curved rate profile (compared with the linear plot obtained with the Monsanto catalyst (*Graph 5- 2*)) was observed (*Graph 5- 1*). The zero order rate constant in the early part of the reaction ($k= 4.12 \times 10^{-4}$ mol l^{-1} s^{-1}) was reproducible. No catalyst precipitation was observed after the reaction. The curvature of the line from the beginning of the reaction may be indicative of catalyst degradation to the Monsanto catalyst, $[Rh(CO)_2(I)_2]^-$ which is formed *in situ* from $[RhCl(CO)_2]_2$. The more pronounced curvature of the line after 4200 s suggests that the reaction becomes first order in methanol at low methanol concentration.



Graph 5- 1: CO uptake against time for $[RhCl(CO)_2]_2$-DTBPMB at 150 °C

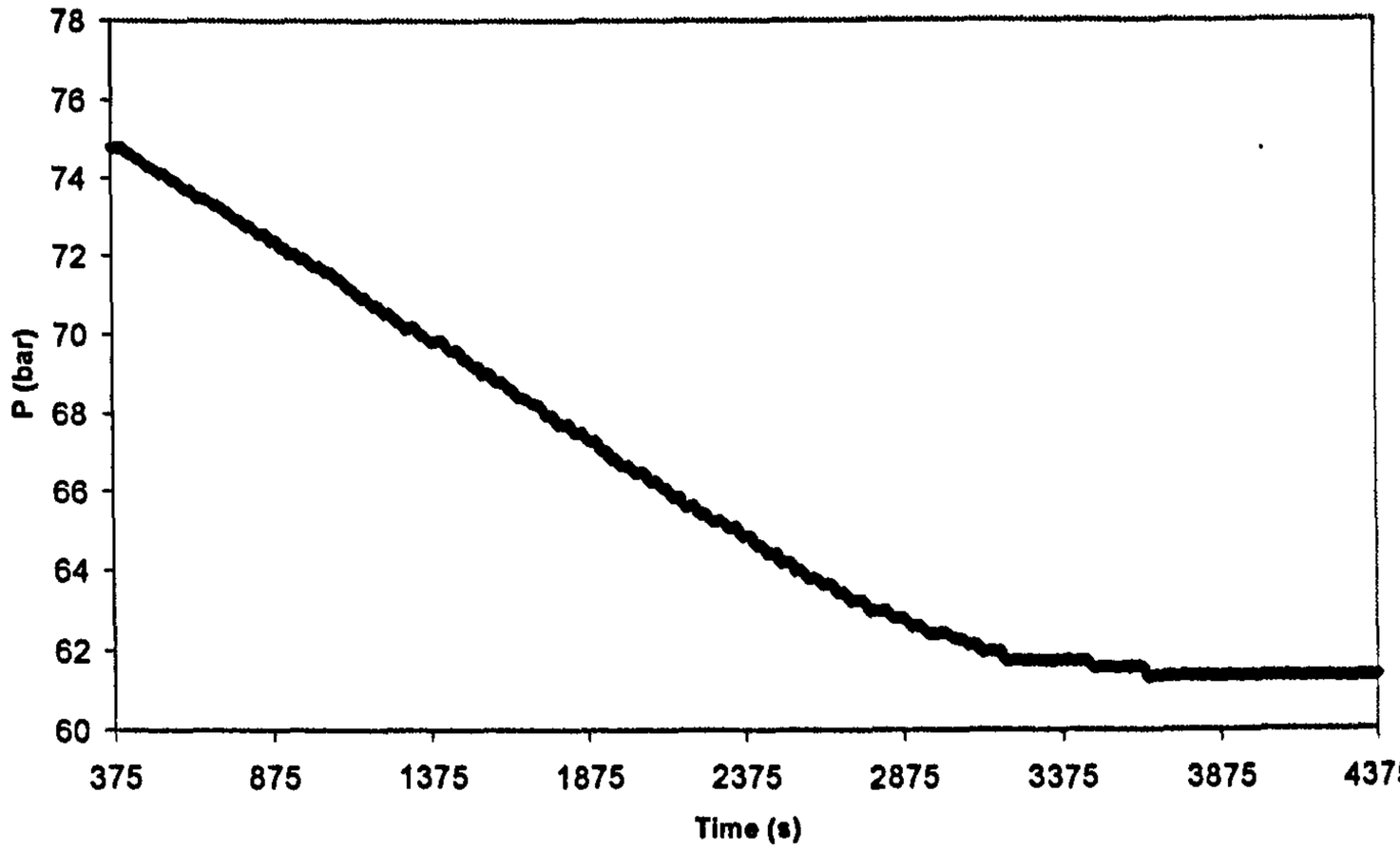
The unmodified $[RhCl(CO)_2]_2$ was tested under the same conditions (150 °C and 27 bar of CO) for comparison. The zero order rate constant observed for the reaction was $k= 2.26 \times 10^{-4}$ mol l^{-1} s^{-1} (*Graph 5- 2*). This reaction was clearly

slower. One possible explanation for the results obtained using DTBPMB is that a more electron rich complex than $[RhI_2(CO)_2]^-$, such as [Rh(DTBPMB)I(CO)] forms at the start of the reaction. Oxidative addition of MeI to this complex is faster than to $[RhI_2(CO)_2]^-$, but it is still rate determining. However, this complex decomposes to $[RhI_2(CO)_2]^-$ over the course of the reaction. Further evidence in favour of this explanation is provided later.



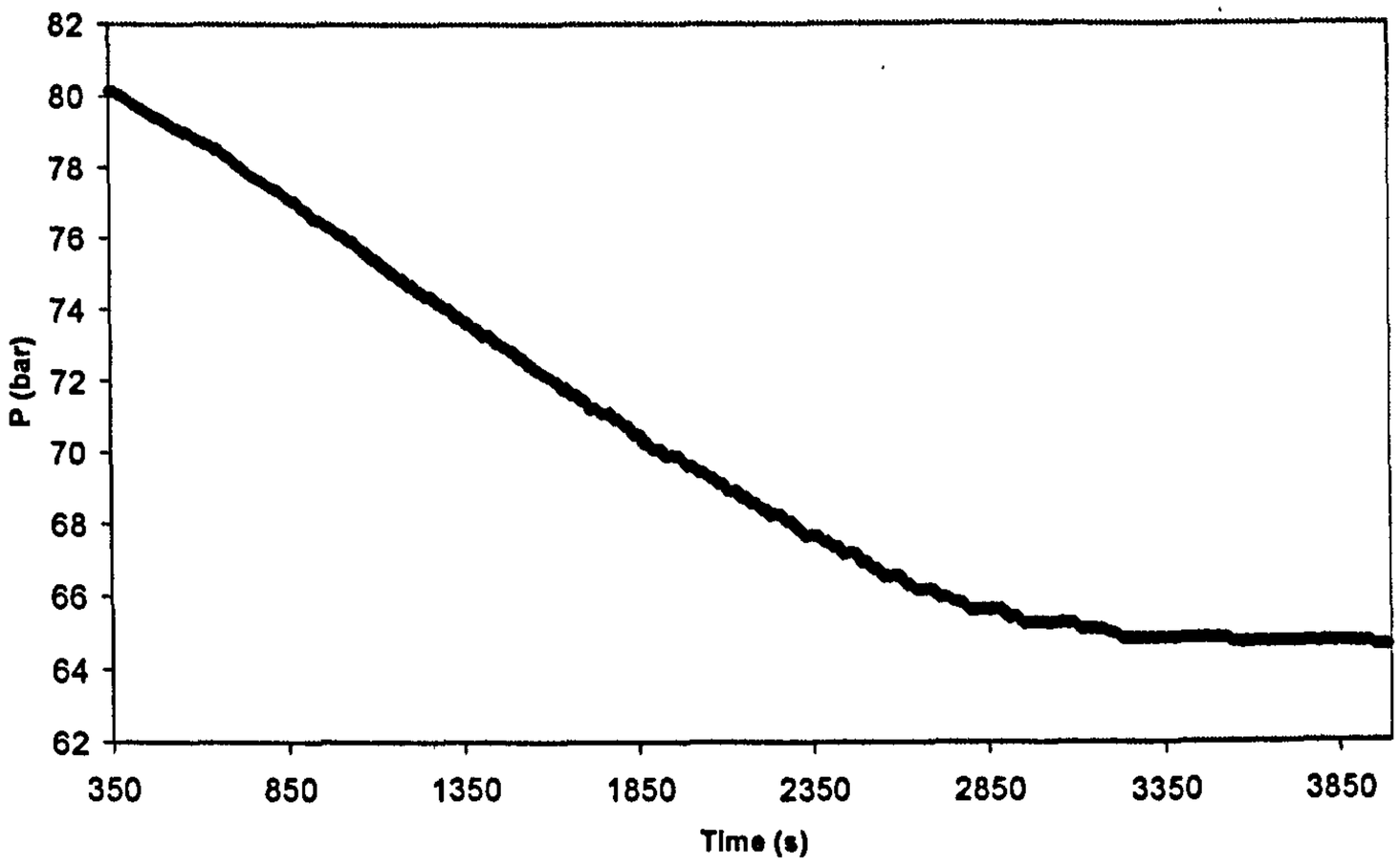
Graph 5- 2: CO uptake against time for unmodified $[RhCl(CO)_2]_2$ at 150 °C

The phosphine modified catalytic system, $[RhCl(CO)_2]_2$/ DTBPMB, was tested under 27 bar of CO at 180 °C. The catalyst showed a higher activity under these conditions, the zero order rate constant being k= 8.90 x 10^{-4} mol l^{-1} s^{-1} (*Graph 5-3*). The straight line observed from the beginning of the reaction suggests that a stable catalyst is formed very early in the reaction.



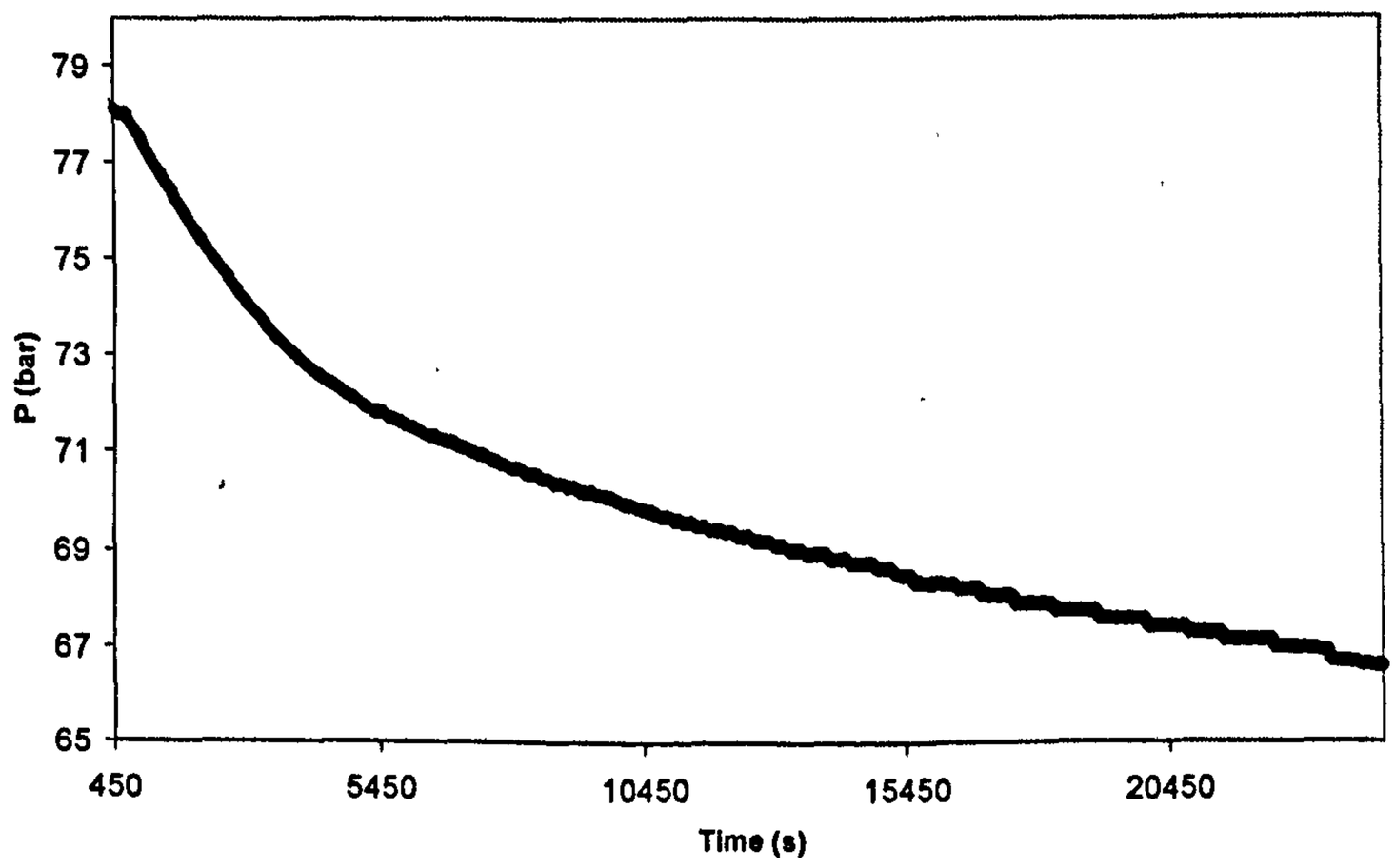
Graph 5- 3: CO uptake against time for $[RhCl(CO)_2]_2$-DTBPMB at 180 °C

To determine if the higher activity was due to the catalyst [Rh(DTBPMB)Cl(CO)] or a rhodium complex formed via deactivation of the starting material, a comparative study was carried out using the unmodified $[RhCl(CO)_2]_2$ under 27 bar of CO at 180 °C. The rate observed was k= 6.09 x 10^{-4} mol l^{-1} s^{-1}(*Graph 5- 4*), suggesting that if the phosphine modified catalyst decomposes at 180 °C, the higher rate observed in the presence of phosphine may be due to the presence of different methyl or iodide species. Free phosphine and methyl iodide will react together to afford the phosphonium salt, $[(Me^tBuP^+CH_2)_2C_6H_4]I_2$. Therefore, the concentration of methyl iodide will decrease leading to a lower rate. However, an increase of the concentration of inorganic iodide usually provokes an increase of the rate. In this particular case, the higher rate observed when the phosphine is present suggests that the effect of the inorganic iodide overrides the effect of the methyl iodide.



Graph 5- 4: CO uptake against time for unmodified $[RhCl(CO)_2]_2$ at 180 °C

At 150 °C the amount of water was reduced from 5.55 x 10^{-2} mol (1 ml) to 9.78 x 10^{-3} mol (0.18 ml) keeping the rest of the reaction conditions unchanged. An initial high rate of 3.80 x 10^{-4} mol l^{-1} s^{-1} was observed (*Graph 5- 5*) but catalyst decomposition again appeared to occur.



Graph 5- 5: CO uptake against time for $[RhCl(CO)_2]_2$-DTBPMB at low water concentration

In view of these results, the characterisation of the species involved in the catalytic cycle and the catalyst stability were studied by HPIR and HPNMR.

5.3. Characterisation of the species involved in the catalytic cycle

5.3.1. High pressure infrared studies in DCM

5.3.1.1. $[RhCl(CO)_2]_2$ and DTBPMB

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in DCM under argon. A new complex was formed almost instantaneously at room temperature (*Figure 5- 1*). The starting material showed two weak carbonyl stretches at 2082 and 2030 cm^{-1}, whereas the final complex exhibited one single carbonyl stretch at 1945 cm^{-1} with a shoulder at 1975 cm^{-1} which has not been assigned. The increase in the temperature to 50 °C resulted in an increase in the intensity on the band corresponding to the rhodium-ligand complex. The decrease in γ_{CO} on addition of DTBPMB indicates an increase of the electron density on the rhodium and therefore of the back donation into the π^* orbital of CO, making the carbon-oxygen bond weaker. The complex was subsequently isolated and fully characterised as [Rh(DTBPMB)Cl(CO)] (see chapter 7)

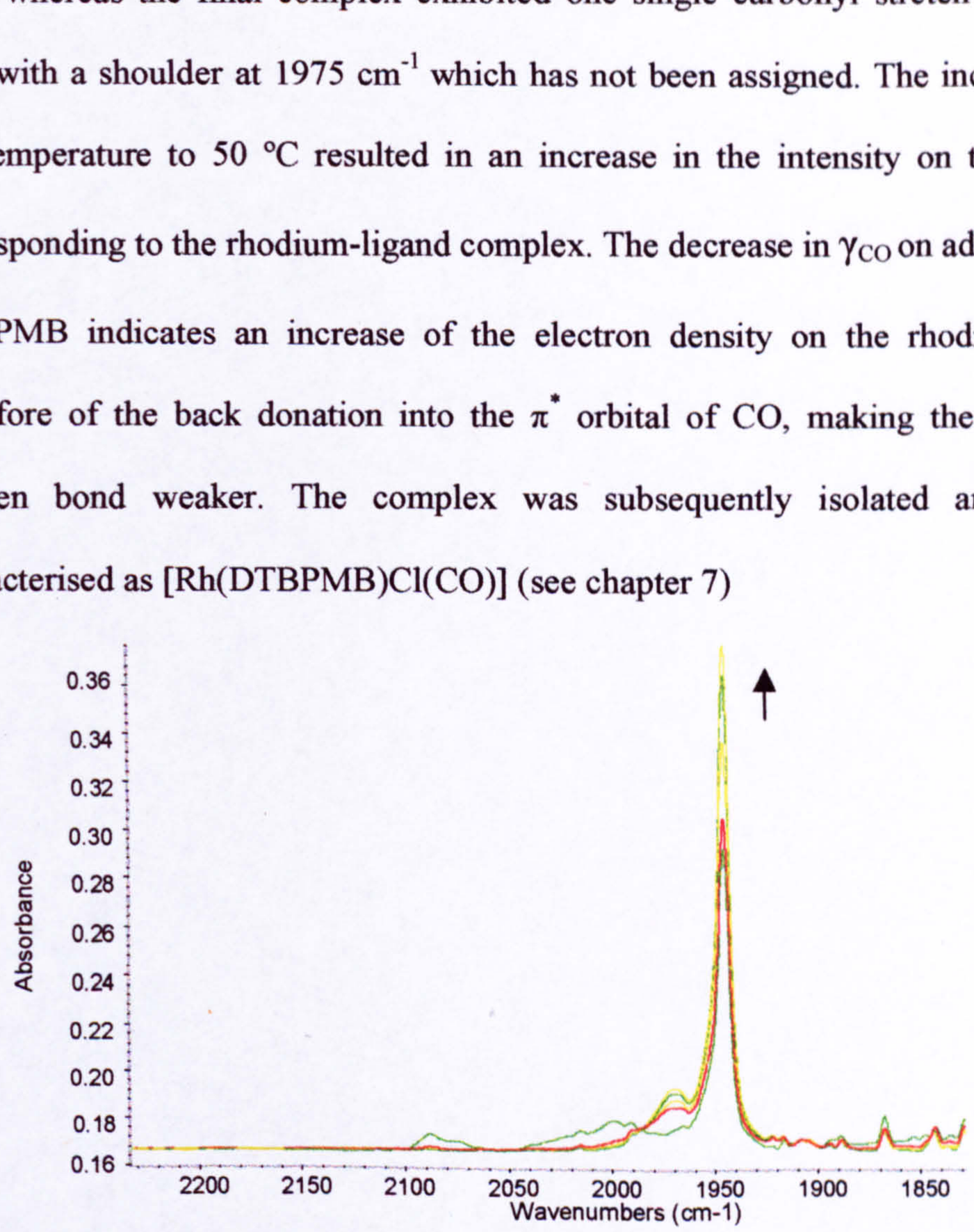


Figure 5- 1: Infrared spectra of a solution of $[RhCl(CO)_2]_2$/DTBPMB in DCM on heating from 20 °C to 50 °C

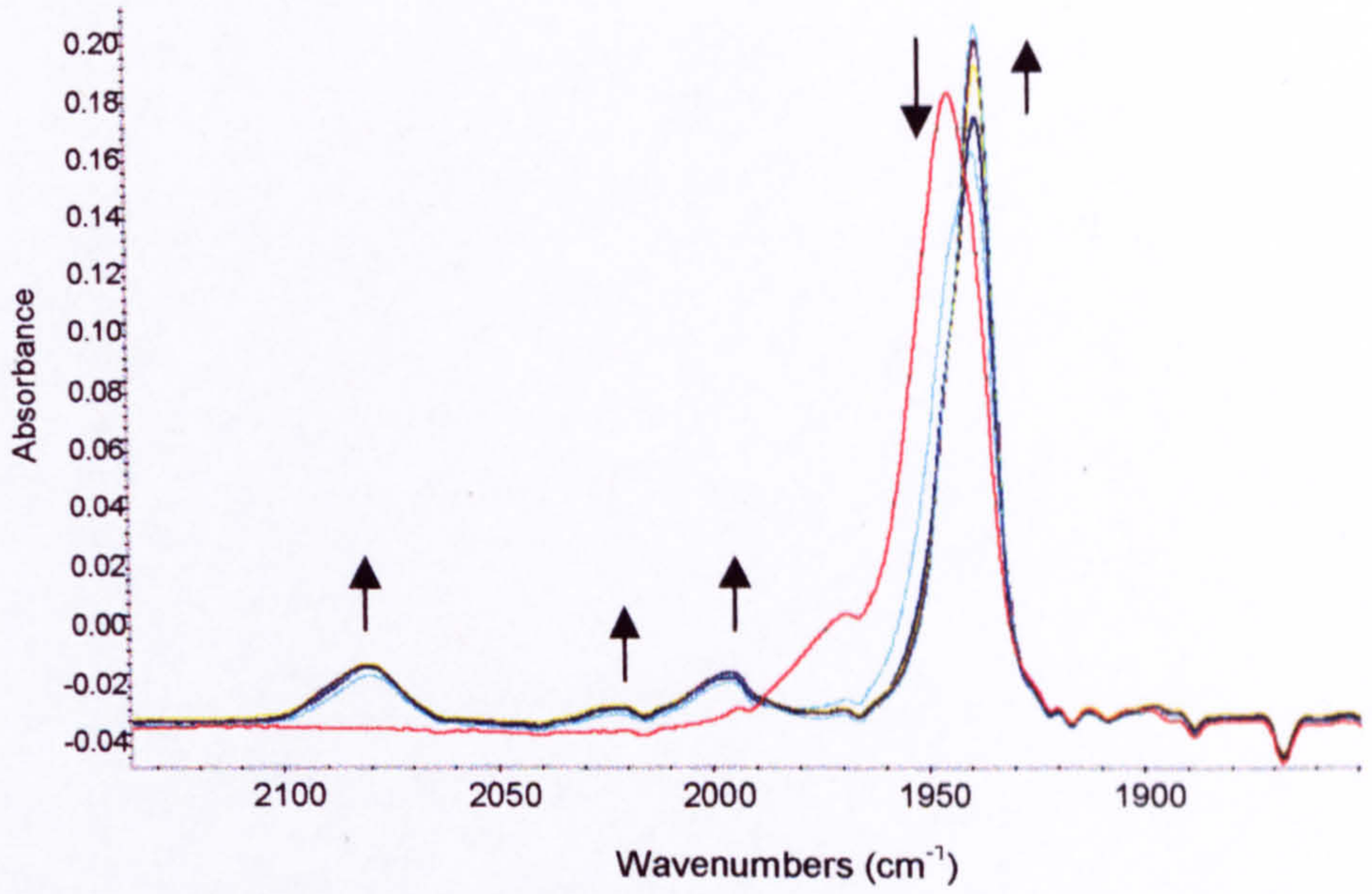


Figure 5-9: Infrared spectra of [Rh(DTBPMB)Cl(CO)] under CO in MeOH at 125 ºC

On addition of methyl iodide an instantaneous decrease on the intensity of the bands at 1938 cm^{-1} and 1992 cm^{-1} occurred, giving rise to two bands at 2058 cm^{-1} and 1993 cm^{-1}, which correspond to the $[RhI_2(CO)_2]^-$ (green arrows in *Figure 5-10*). This is the species expected from the unmodified catalyst since oxidative addition of methyl iodide to the $[RhI_2(CO)_2]^-$ is rate determining.

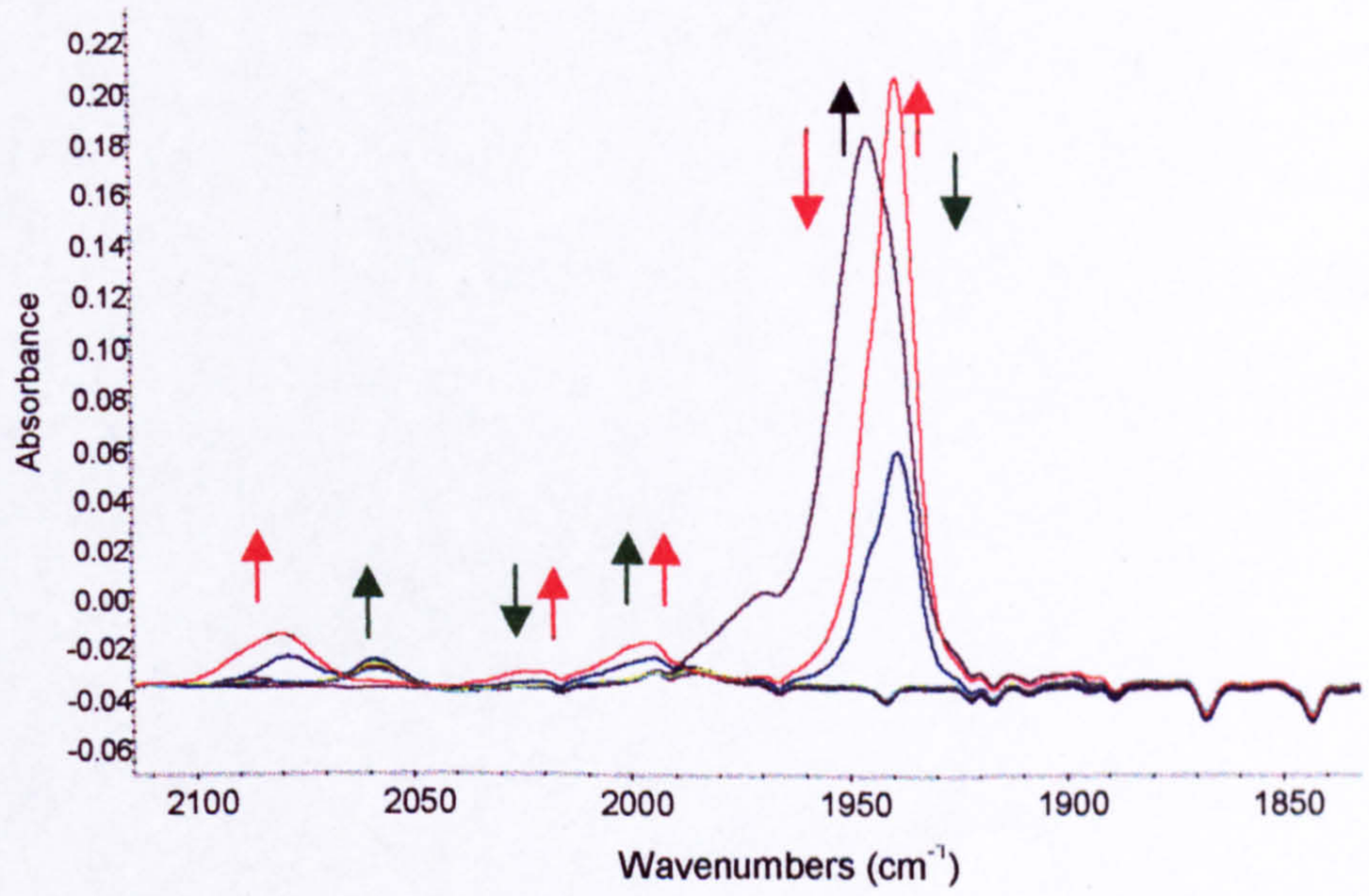


Figure 5-10: Infrared spectra of [Rh(DTBPMB)Cl(CO)$_2$] under CO in MeOH in the presence of methyl iodide at 125 ºC.

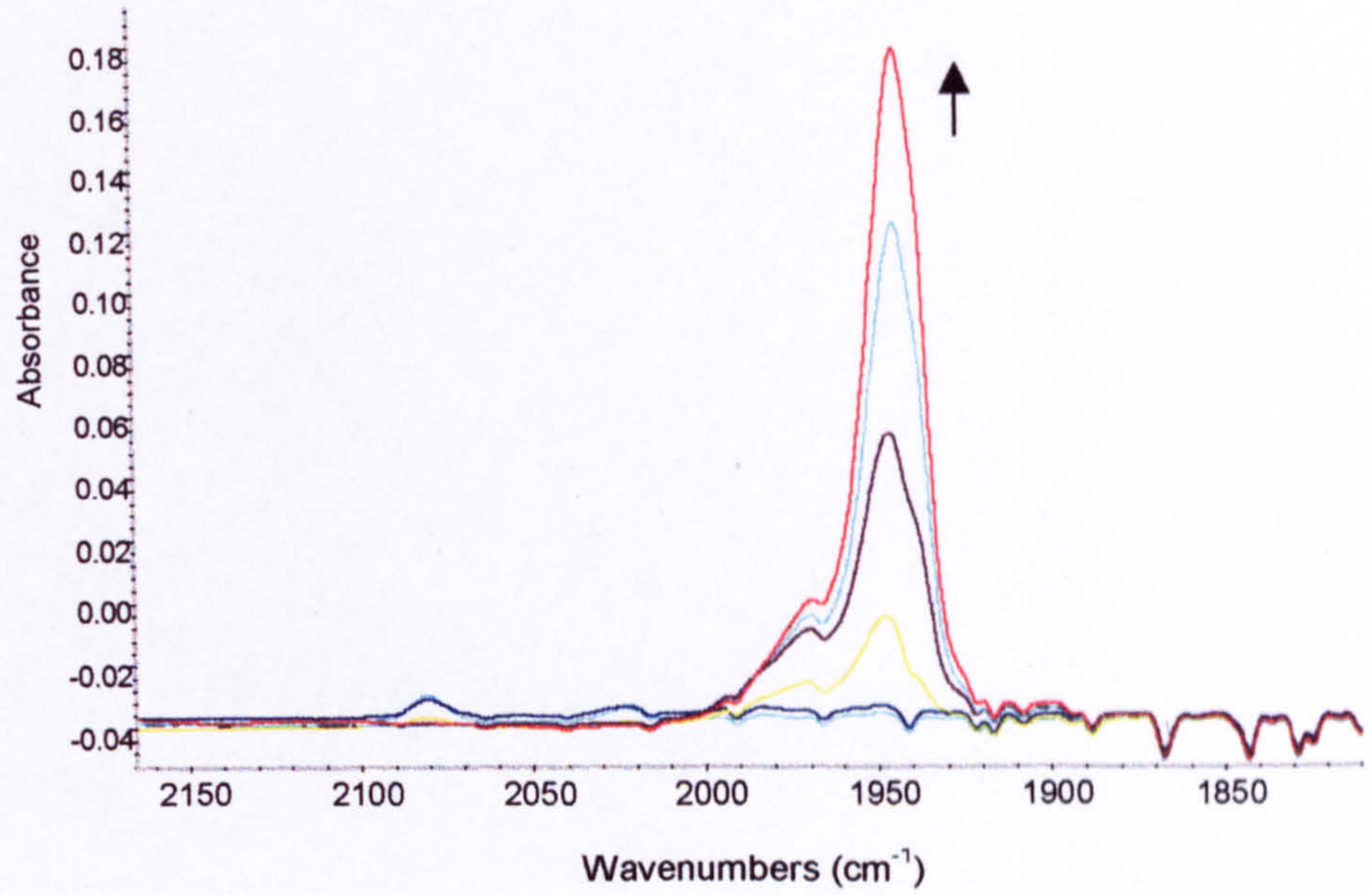


Figure 5-8: Infrared spectra of $[RhCl(CO)_2]_2$/DTBPMB in MeOH at 120 °C

The addition of CO at 125 °C shifted the band from 1945 cm^{-1} to 1938 cm^{-1} and three weak bands at 2082, 2030 and 1992 cm^{-1} arose. The bands at 1938 cm^{-1} and 1992 cm^{-1} are tentatively attributed to the complex containing two carbonyl groups, $[Rh(DTBPMB)Cl(CO)_2]$. Similar rhodium complexes of PEt_3, such as $[RhCl(CO)_2(PEt_3)_2]$[13] or $[RhI(CO)_2(PEt_3)_2]$[10], have been reported by Cole-Hamilton and coworkers to be formed by reaction of the monocarbonyl, $[Rh(PEt_3)_2X(CO)]$, and CO. The chloro-rhodium-dicarbonyl showed a strong band at 1936 cm^{-1} and a weak band at 1992 cm^{-1}, whereas the iodo-rhodium-dicarbonyl showed a strong band at 1943 cm^{-1} and a weak band at 1999 cm^{-1}. The bands at 2082 and 2030 cm^{-1} correspond to the formation of $[RhCl(CO)_2]_2$ from [Rh(DTBPMB)Cl(CO)] by loss of DTBPMB.

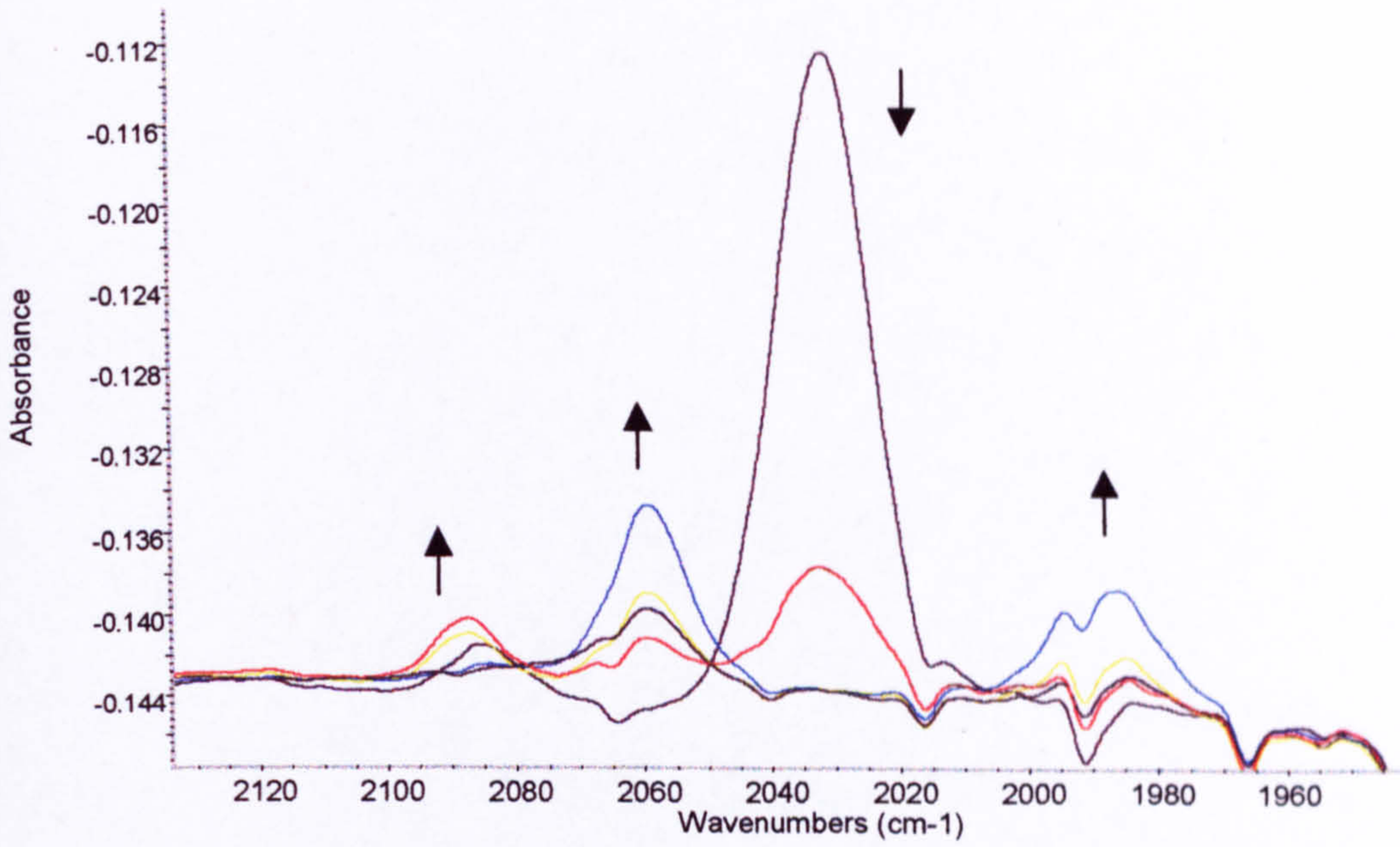


Figure 5-7: HPIR spectra $[RhCl(CO)_2]_2$/DTBPMB/MeI/MeOH under CO at 120 ℃

5.3.2. High pressure infrared studies in methanol

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in MeOH under argon. The solution was introduced via cannula in the high pressure infrared cell. At room temperature only the initial $[RhCl(CO)_2]_2$, which shows two weak carbonyl stretches at 2082 and 2030 cm^{-1}, was present in solution. The complex [Rh(DTBPMB)Cl(CO)], which exhibits one single carbonyl stretch at 1945 cm^{-1} with an unidentified shoulder at 1975 cm^{-1}, was formed after 20 minutes at 90 ℃. The increase in the temperature to 120 ℃ resulted only in an increase in the intensity on the band corresponding to this Rh(I) complex (*Figure 5-8*).

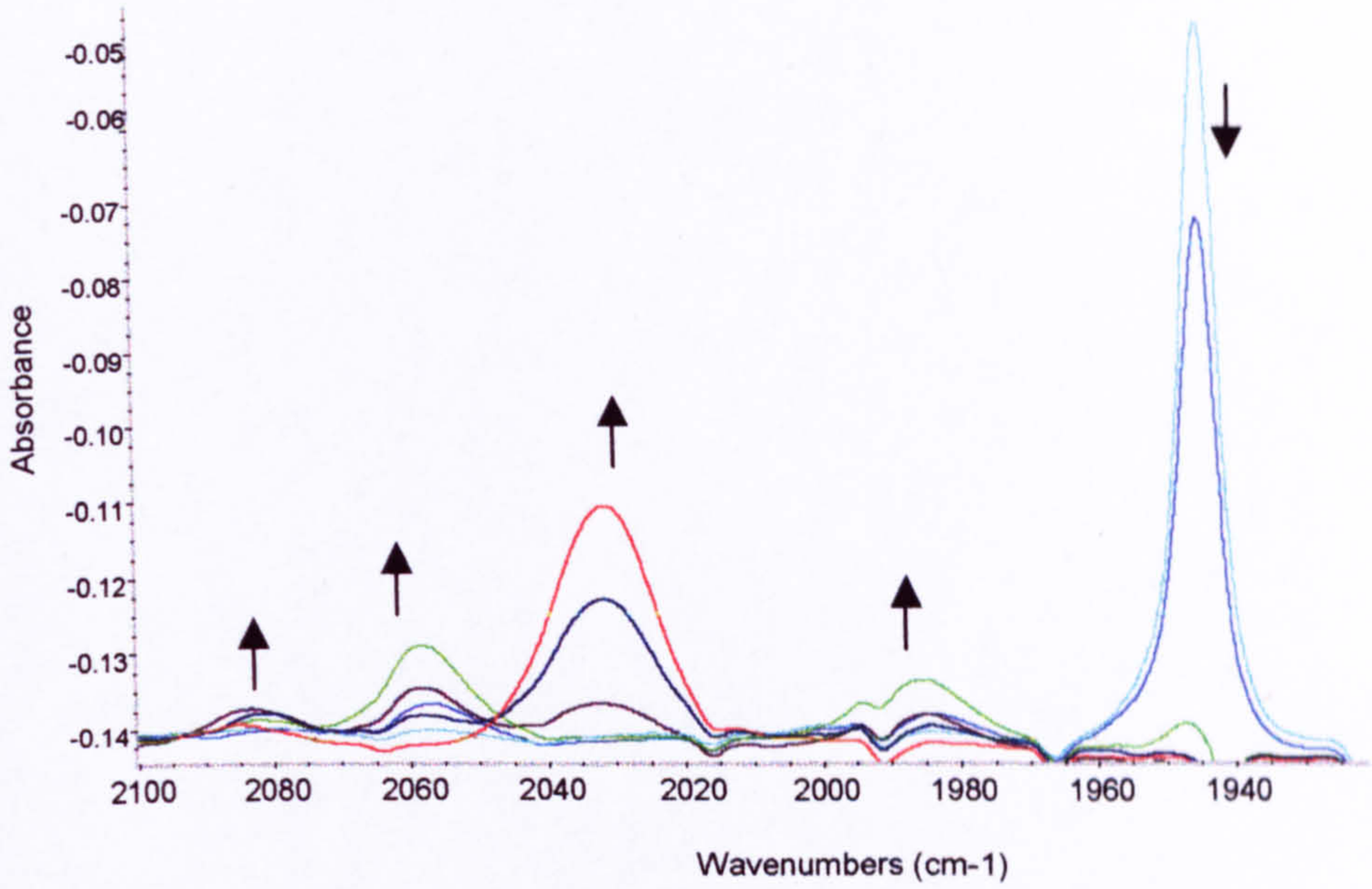


Figure 5-6: HPIR spectra of $[RhCl(CO)_2]_2$/DTBPMB/MeI under CO in DCM

When MeOH was added, the band at 2031 cm^{-1} disappeared after ten minutes whilst the band at 2084 cm^{-1} shifted to 2088 cm^{-1}. The band at 2088 cm^{-1} could be attributed to $[RhI_4(CO)_2]^-$ (γ_{CO}= 2090 cm^{-1}).[5] The bands corresponding to $[RhI_2(CO)_2]^-$ (2059 cm^{-1} and 1994 cm^{-1}) increased. These results suggest that the catalyst is not stable under the reaction conditions, since the addition of methanol promotes the decomposition of the acyl complex yielding the non-modified rhodium complex, which is then responsible for the catalysis (*Figure 5-7*).

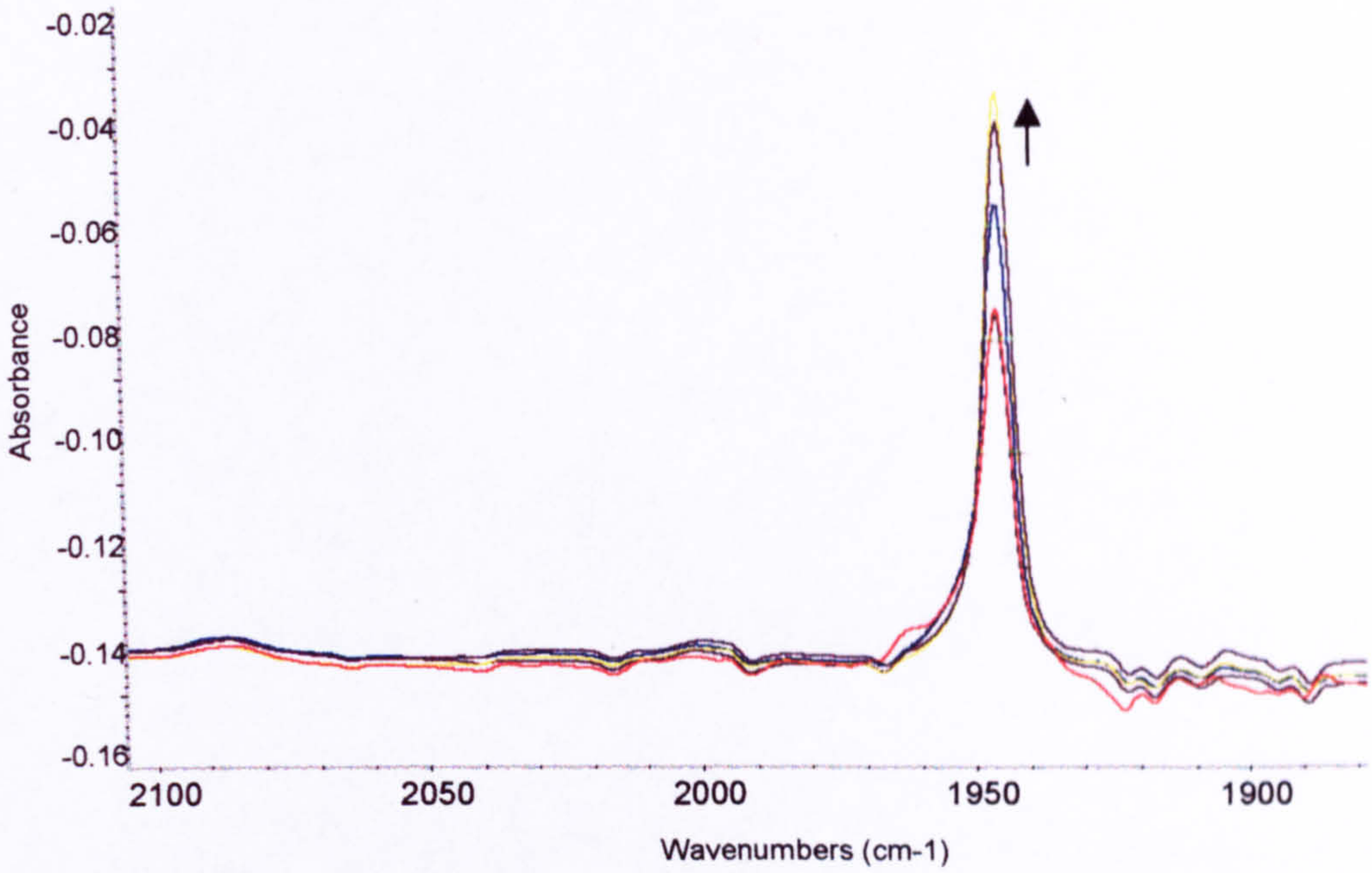


Figure 5-5: Infrared spectra of $[RhCl(CO)_2]_2$ and DTBPMB under CO on heating from 20 ℃ to 120 ℃

The temperature was held at 120 ℃ for 1 hour without any appreciable change in the band at 1945 cm^{-1}. Methyl iodide was then added to the solution. The spectrum obtained immediately after the addition showed an unaltered band at 1945 cm^{-1}. However, one minute after the addition, the band at 1945 cm^{-1} decreased slightly and two new bands at 2031 cm^{-1} and 2084 cm^{-1} arose (*Figure 5-6*). In addition, bands at 2059, 1994 and 1986 cm^{-1} arose. The band at 2031 cm^{-1} is attributed to the oxidative addition product $[Rh(DTBPMB)(CH_3)(I)_2(CO)]$ whereas the band at 2084 cm^{-1} is attributed to the migratory insertion acyl product $[Rh(DTBPMB)(COCH_3)(I)_2(CO)]$. The bands at 2059 cm^{-1} and 1994 cm^{-1} seems to correspond to the diiodide-dicarbonyl-rhodium anion, $[RhI_2(CO)_2]^-$, which exhibit bands at 2058 cm^{-1} and 1993 cm^{-1}.[5] The band at 1986 cm^{-1} has not been assigned.

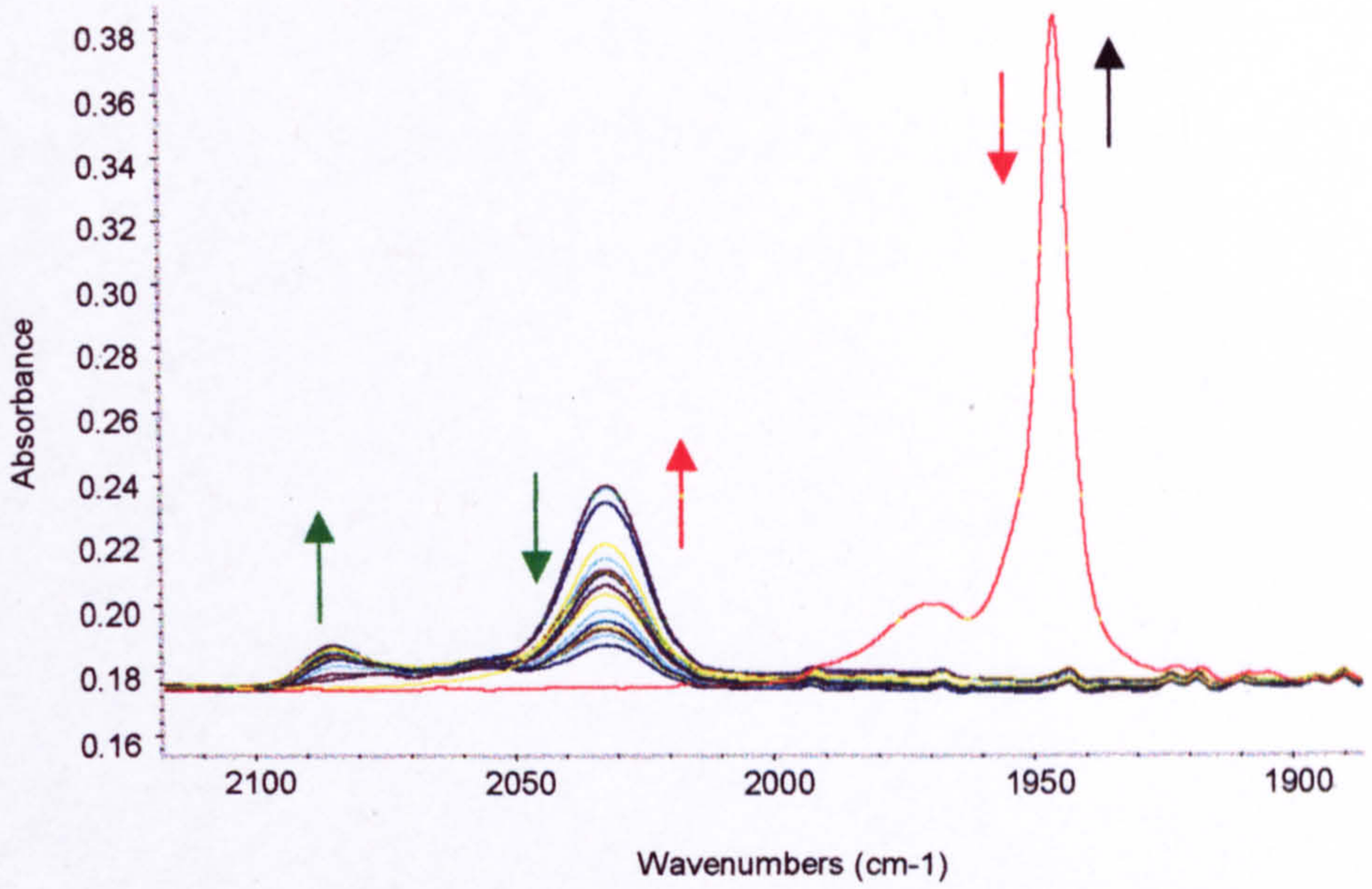


Figure 5- 4: Infrared spectra of the species involved in the catalytic cycle

5.3.1.5. $[RhCl(CO)_2]_2$ and DTBPMB under CO.

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in DCM under argon. The solution was introduced via cannula in the high pressure infrared cell, which was placed in the spectrometer and pressurised with 27 bar of CO. The temperature was gradually increased form 20 °C to 120 °C. At all temperatures the infrared spectra exhibit one single carbonyl stretch at 1945 cm^{-1}, which is attributed to the formation of the Rh(I) complex [Rh(DTBPMB)Cl(CO)] (*Figure 5-5)*.

The shift from 2031 cm^{-1} to 2084 cm^{-1} observed for [Rh(DTBPMB)I_2(CO)(CH_3)] on addition of CO to form [Rh(DTBPMB)I_2($COCH_3$)(CO)] is in good agreement with previous studies carried out for other systems.

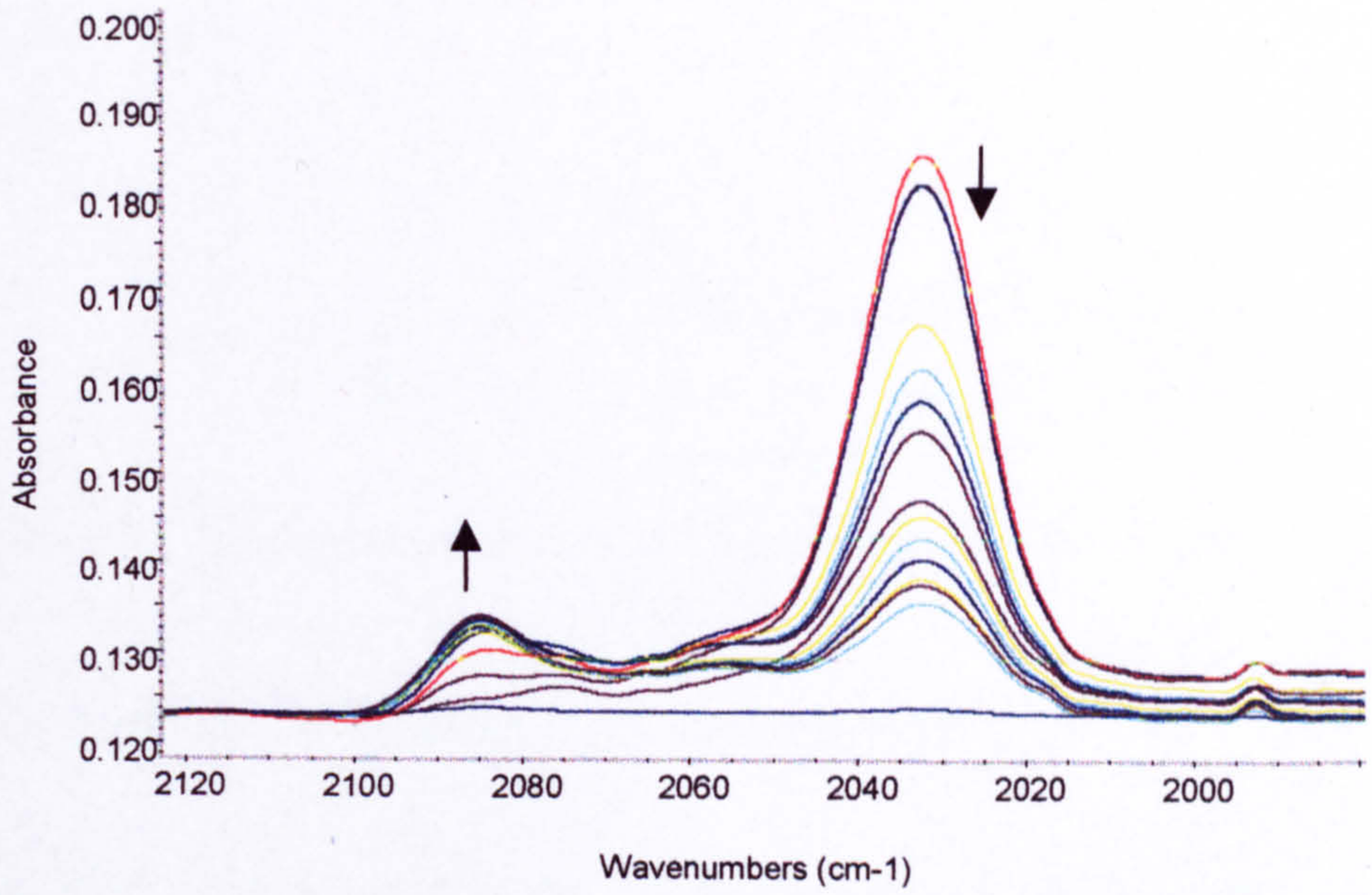


Figure 5- 3: Infrared spectra of $[RhCl(CO)_2]_2$ DTBPMB/ MeI under CO in DCM at 130 °C

5.3.1.4. Summary of the infrared studies in DCM

The complex [Rh(DTBPMB)Cl(CO)] exhibits one band at 1945 cm^{-1} (black arrow in *Figure 5- 4*). Oxidative addition of methyl iodide to form the Rh(III) complex [Rh(DTBPMB)$(I)_2$(CO)(CH_3)] occurred at 90 °C. At this temperature the intensity of the band at 1945 cm^{-1} decreased and a new band at 2031 cm^{-1} arose (red arrows in *Figure 5- 4*). Increasing the temperature to 120 °C the formation of this complex was accelerated. The cell was pressurised with 27 bar of CO at 120 °C. After 15 minutes the intensity of the band at 2031 cm^{-1} decreased and at the same time a new band at 2084 cm^{-1} appeared (green arrows in *Figure 5- 4*). This temperature was held for 160 minutes when the band reached its highest intensity (*Figure 5- 4*).

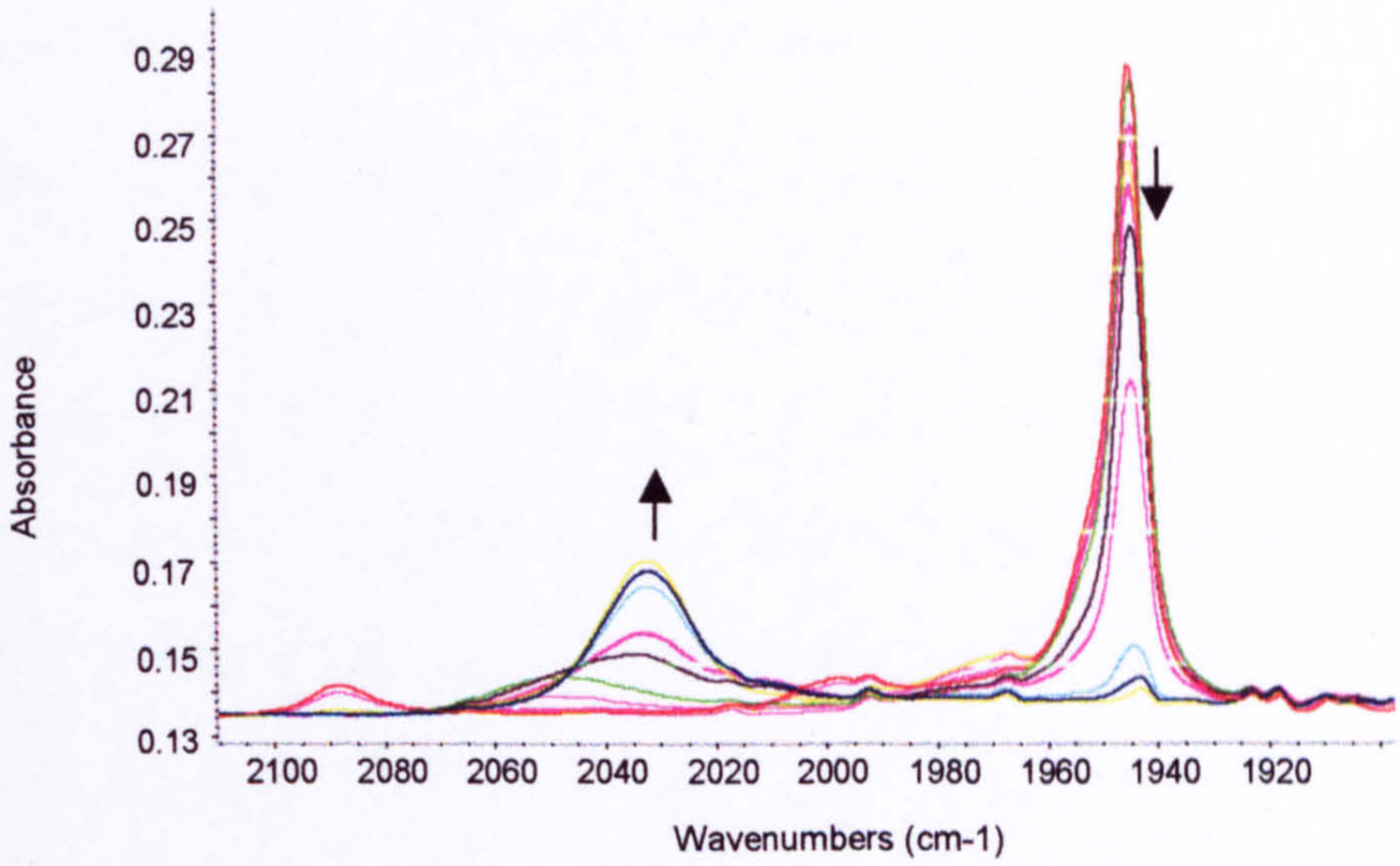


Figure 5- 2: Infrared spectra of $[RhCl(CO)_2]_2$/ DTBPMB/ MeI in DCM on heating from 20 ℃ to 120 ℃

5.3.1.3. [Rh(DTBPMB)$(I)_2(CH_3)(CO)$] under CO

The HPIR cell containing the solution of the Rh(III) complex tentatively assigned as [Rh(DTBPMB)$I_2(CO)(CH_3)$] at 120 °C was pressurised with 30 bar of CO. This temperature was held for 30 minutes and no change was observed. The temperature was then increased to 130 °C for 15 minutes. Under these conditions the band at 2031 cm^{-1} decreased whilst a band at 2084 cm^{-1} appeared. This band is tentatively attributed to the metal acyl complex [Rh(DTBPMB)$I_2(COCH_3)(CO)$], in which the electron density on the rhodium is lower than in the complex [Rh(DTBPMB)$I_2(CO)(CH_3)$] (*Figure 5- 3*). Cole-Hamilton and coworkers showed for the Rh-PEt_3 system that addition of CO to the Rh (III) complex [Rh$(CH_3)I_2(CO)(PEt_3)_2$] (γ_{CO}= 2043 cm^{-1}) led to the formation of the Rh-acyl complex [Rh$(COCH_3)I_2(CO)(PEt_3)_2$], which exhibit two CO stretches, γ_{CO}= 2065 cm^{-1} (Rh*CO*) and γ_{CO}= 1665 cm^{-1} (Rh*COCH*$_3$).[10]

5.3.1.2. $[RhCl(CO)_2]_2$/ DTBPMB and methyl iodide

Methyl iodide was added to the solution in the high pressure infrared cell at room temperature. The complex [Rh(DTBPMB)Cl(CO)] underwent exchange of chlorine by iodine to form [Rh(DTBPMB)I(CO)]. The latter complex was also isolated and fully characterised (see chapter 7). Either [Rh(DTBPMB)Cl(CO)] or [Rh(DTBPMB)I(CO)] exhibit one band at 1945 cm^{-1}.

For a solution of $[RhCl(CO)_2]_2$/ DTBPMB/ MeI at room temperature only the band at 1945 cm^{-1} was observed. The temperature was gradually increased to 120 °C. At this temperature the band at 1945 cm^{-1} decreased its intensity whilst a new band at 2031 cm^{-1} arose. This new band is tentatively assigned to the Rh (III) complex $[Rh(DTBPMB)I_2(CO)(CH_3)]$ formed by the oxidative addition of MeI to [Rh(DTBPMB)I(CO)] (*Figure 5- 2*). In this complex the metal centre is highly nucleophilic, which is important for oxidative addition to occur. The increase on the CO stretch frequency agrees with a decrease of the electron density in a Rh(III) from a Rh(I) centre, since the back donation into the carbonyl is lower and therefore the CO bond is stronger. Previous studies on the carbonylation of methanol catalysed by the electron rich Rh-PEt_3 complexes showed that oxidative addition of methyl iodide to $[RhI(CO)(PEt_3)_2]$ (Rh(I) complex) to form $[Rh(CH_3)I_2(CO)(PEt_3)_2]$ (Rh(III) complex) led to a shift of the CO stretch frequency from 1961 cm^{-1} to 2043 cm^{-1}.[10] Thus, our findings are in good agreement with the formation of the Rh (III) complex, $[Rh(DTBPMB)I_2(CO)(CH_3)]$, from the Rh(I), [Rh(DTBPMB)I(CO)], by oxidative addition of MeI.

5.3.3.High pressure NMR studies.

5.3.3.1. $[RhCl(CO)_2]_2$ and DTBPMB in d^2-DCM

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in d^2-DCM under argon. The solution was introduced under inert atmosphere into the NMR tube. The ^{31}P NMR spectrum (*Figure 5-11*) showed two doublets of doublets at 62.4 ppm (J_{Rh-P}= 170.8 Hz, J_{P-P}= 31.9 Hz) and 22.5 ppm (J_{Rh-P}= 123.2 Hz, J_{P-P}= 31.9 Hz). The coupling constant J_{Rh-P} observed is in agreement with a Rh(I) complex, whereas the coupling constant J_{P-P} observed suggest that the two phosphorus atoms occupy cis relative position to one another. Thus, this ^{31}P NMR spectrum is attributed to the complex [Rh(DTBPMB)Cl(CO)], whose crystal structure is shown in *Illustration 5- 1* and it is discussed in section 5.3.4.

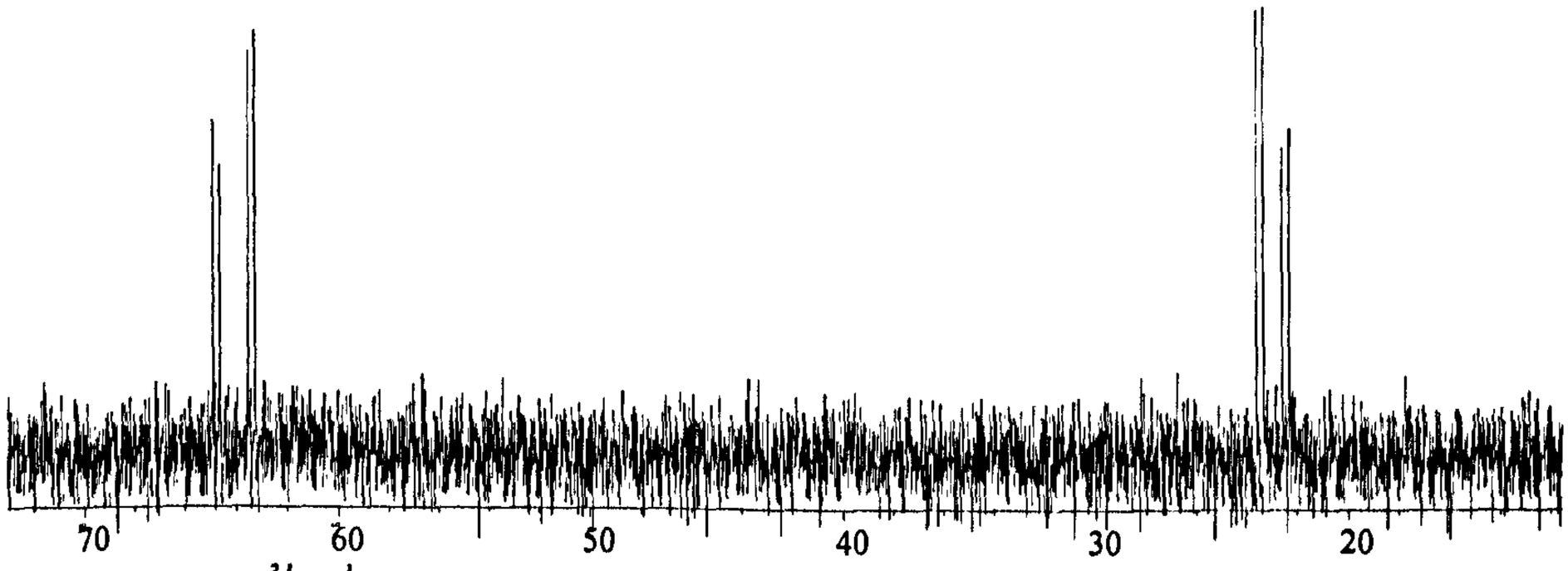


Figure 5-11: $^{31}P\{^1H\}$ NMR spectrum of $[RhCl(CO)_2]_2$ and DTBPMB in CD_2Cl_2 at 20 °C

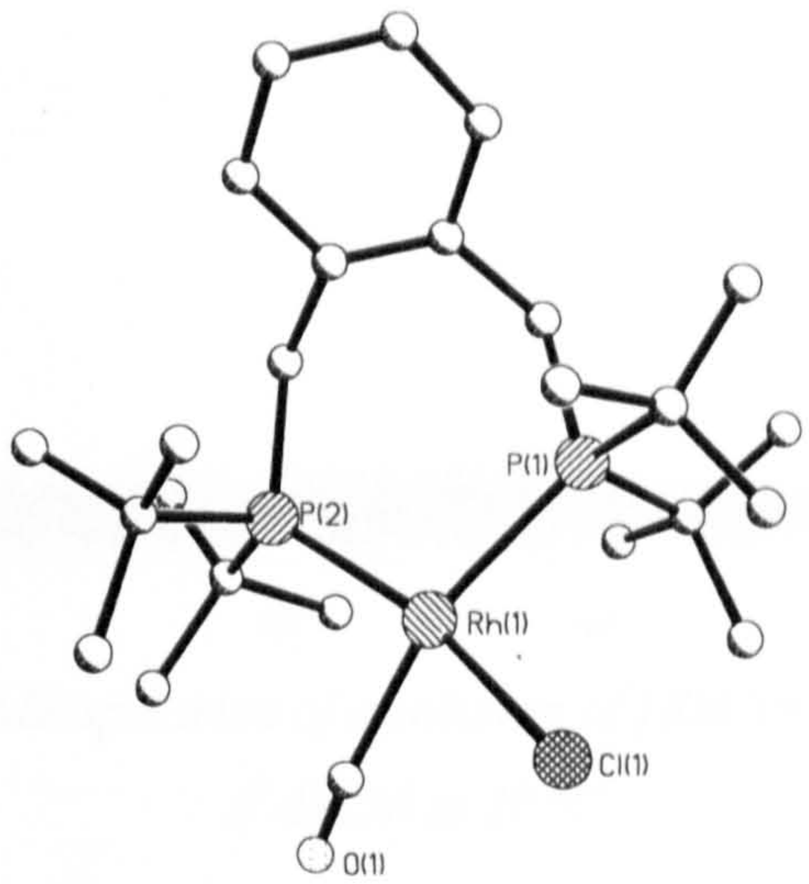


Illustration 5- 1: Crystal structure of [Rh(DTBPMB)Cl(CO)]

5.3.3.2. $[RhCl(CO)_2]_2$, DTBPMB and methyl iodide in d^2-DCM

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in d^2-DCM under argon. Methyl iodide was added to the solution, which was transferred under inert atmosphere into the HPNMR cell. The ^{31}P NMR spectrum showed two doublets of doublets at 62.4 ppm (J_{Rh-P}= 170.8 Hz, J_{P-P}= 31.9 Hz) and 22.5 ppm (J_{Rh-P}= 123.2 Hz, J_{P-P}= 31.9 Hz) for the complex [Rh(DTBPMB)Cl(CO)] (*Figure 5-12*), and two doublets of doublets at 60.4 ppm (J_{Rh-P}= 173.8 Hz, J_{P-P}= 32.7 Hz) and 25.6 ppm (J_{Rh-P}= 128.5 Hz, J_{P-P}= 32.7 Hz). The coupling constant J_{Rh-P} observed suggests that the complex formed contains Rh(I) rather than Rh(III) (the coupling constant J_{Rh-P} would be around 100 Hz) and therefore this spectrum was assigned to the complex [Rh(DTBPMB)I(CO)] produced by exchange of chlorine by iodine (*Figure 5-13*). At 80 °C only the signals due to [Rh(DTBPMB)I(CO)] could be observed. The crystal structure for this complex is shown in *Illustration 5- 2* and discussed in section 5.3.4.

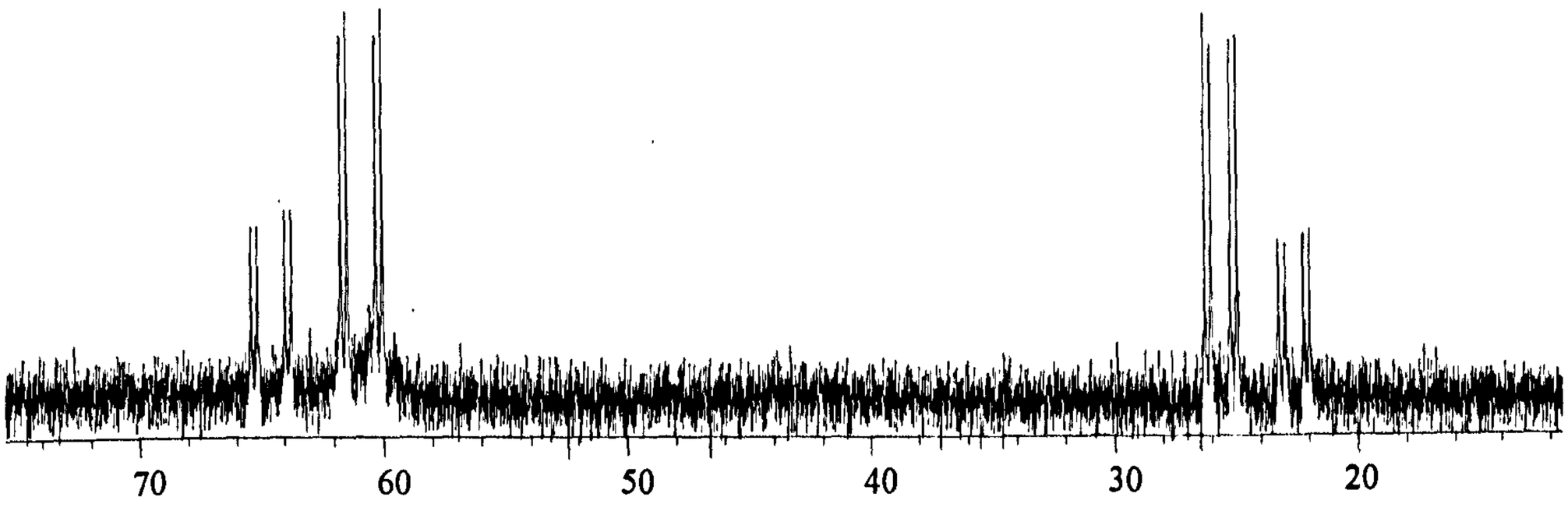


Figure 5-12: $^{31}P\{^{1}H\}$ NMR spectrum of a solution of $[RhCl(CO)_2]_2$/ DTBPMB/ MeI in d^2-DCM at 20 °C

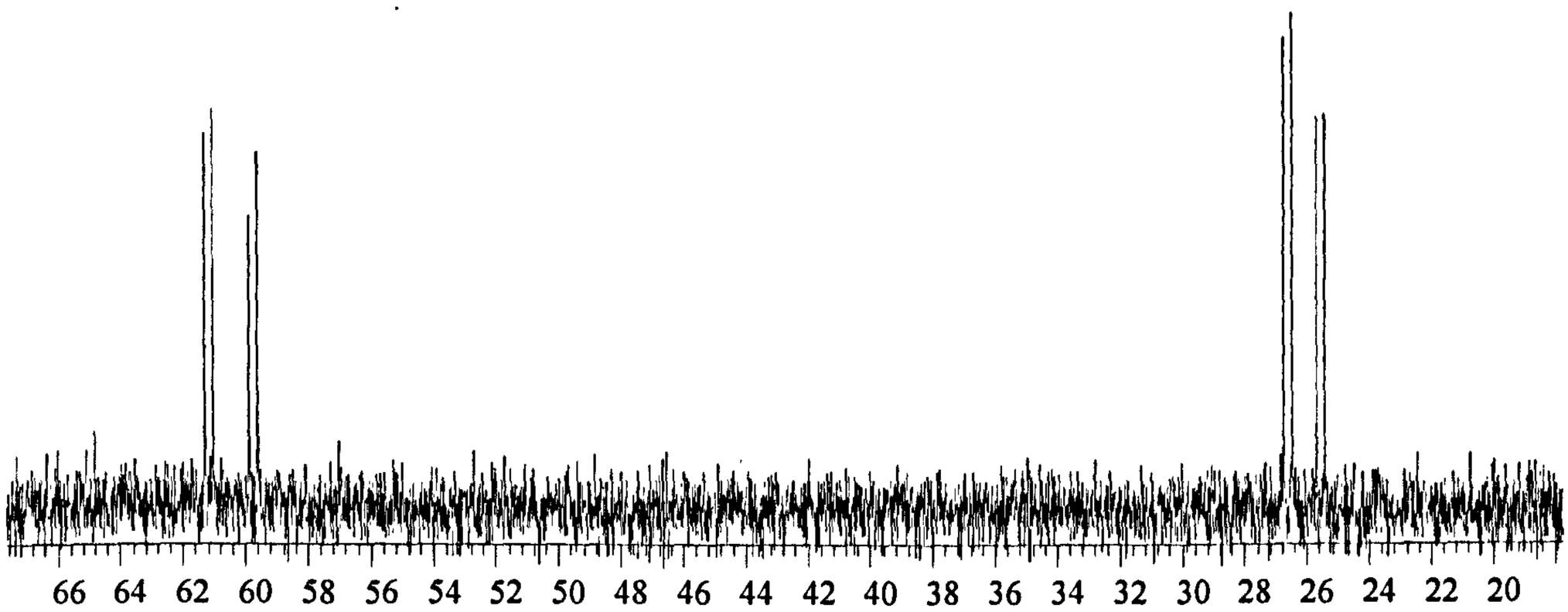


Figure 5-13: $^{31}P\{^{1}H\}$ NMR spectrum of solution of $[RhCl(CO)_2]_2$/ DTBPMB/ MeI in d^2-DCM at 20 °C

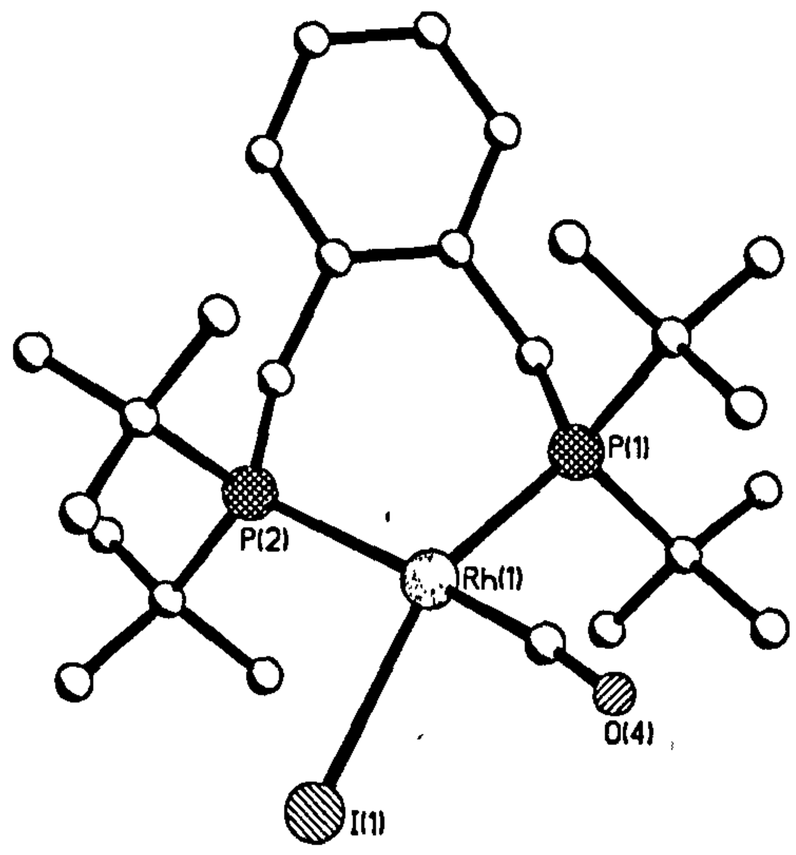


Illustration 5- 2: Crystal structure of [Rh(DTBPMB)I(CO)]

The temperature was raised to 110 °C. At this temperature only a broad singlet at 50.6 ppm due to the phosphonium salt was observed.

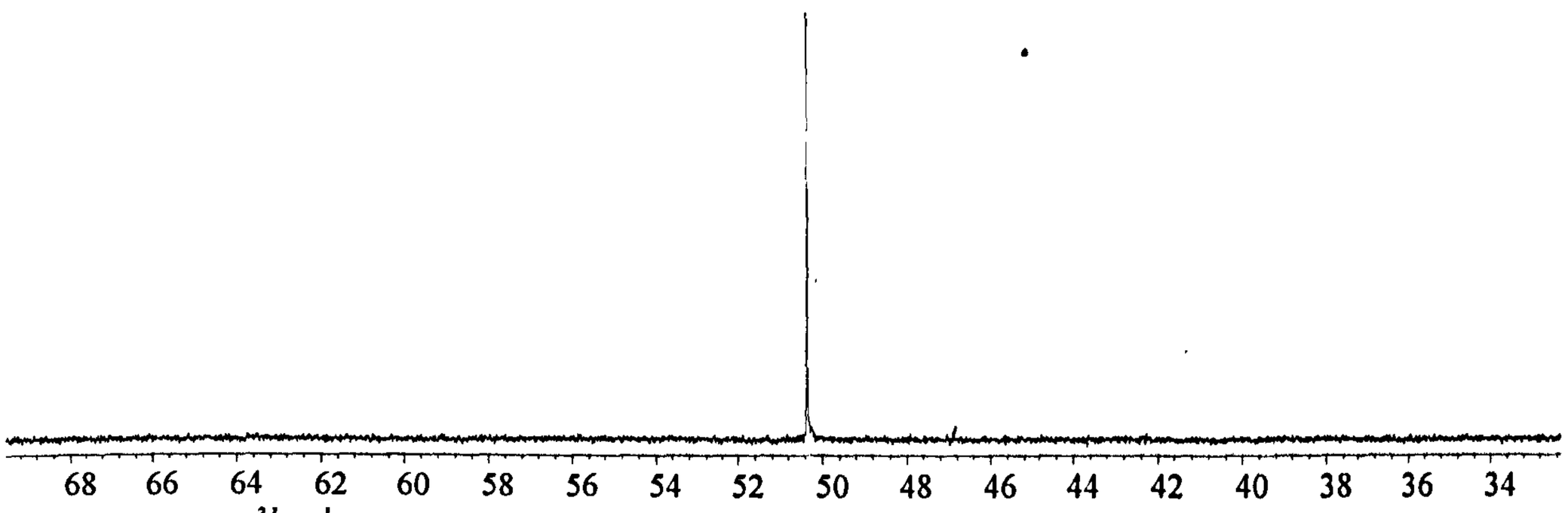


Figure 5-14: $^{31}P\{^{1}H\}$ NMR spectrum of a solution of $[RhCl(CO)_2]_2$/DTBPMB/MeI under CO in d^2-DCM at 110 °C

After slow recrystallisation at room temperature, big red crystals of the phosphonium salt grew. Surprisingly, the corresponding anions to the quaternised phosphorus atoms were not iodide, but triiodide. The crystal structure is shown in *Illustration 5- 3*. This form of the iodine is well known, although quite unusual and not many reports could be found in the literature.

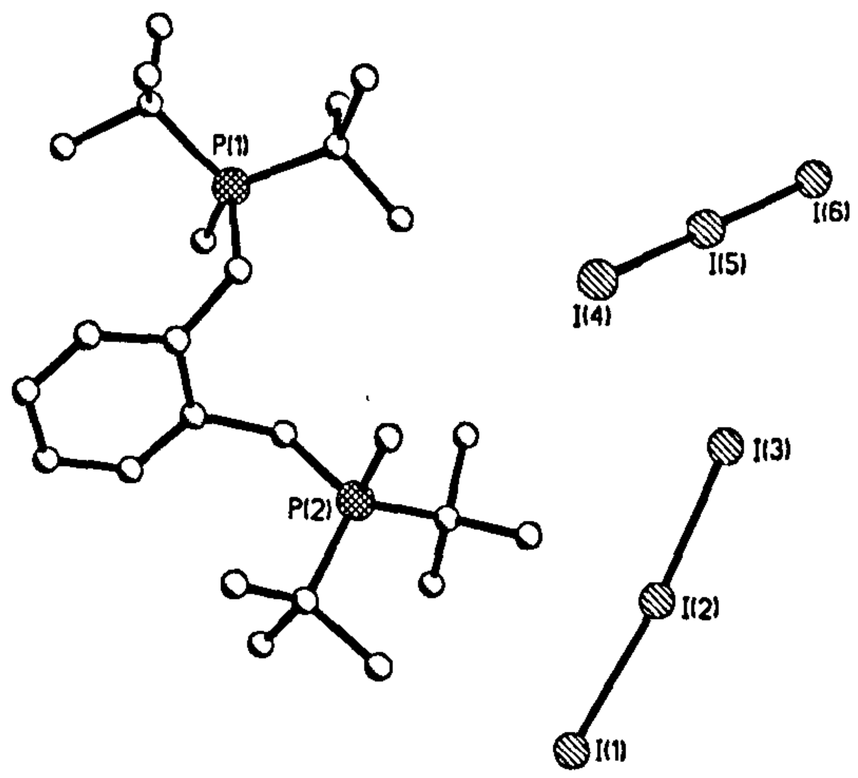


Illustration 5- 3: Crystal structure of $[(DTBPMB)(CH_3)_2]^{2+}(I_3)_2^-$

5.3.3.3. $[RhCl(CO)_2]_2$, DTBPMB and CO in d^2-DCM

The ^{31}P NMR spectrum of a solution of $[RhCl(CO)_2]_2$ and DTBPMB under CO (*Figure 5-15*) showed two doublets of doublets at 62.4 ppm (J_{Rh-P}= 170.8 Hz, J_{P-P}= 31.9 Hz) and 22.5 ppm (J_{Rh-P}= 123.2 Hz, J_{P-P}= 31.9 Hz) for the complex [Rh(DTBPMB)Cl(CO)]. The spectrum also showed a doublet at 60.9 ppm (J_{Rh-P}= 122.5 Hz) and a broad doublet at 60.4 ppm (J_{Rh-P}= 124.7 Hz). The complex arising from the oxidative addition of CD_2Cl_2 to [Rh(DTBPMB)Cl(CO)], [Rh(DTBPMB)(CO)$(Cl)_2(CD_2Cl)$], could be responsible of one of the doublets. The other one could arise from the formation of the dinuclear species $[RhCl(DTBPMB)]_2$, although it is very unlikely under high pressure of CO. Unfortunately, the addition of methyl iodide is not possible when the cell is under pressure and therefore no data of the oxidative addition under these conditions were obtained.

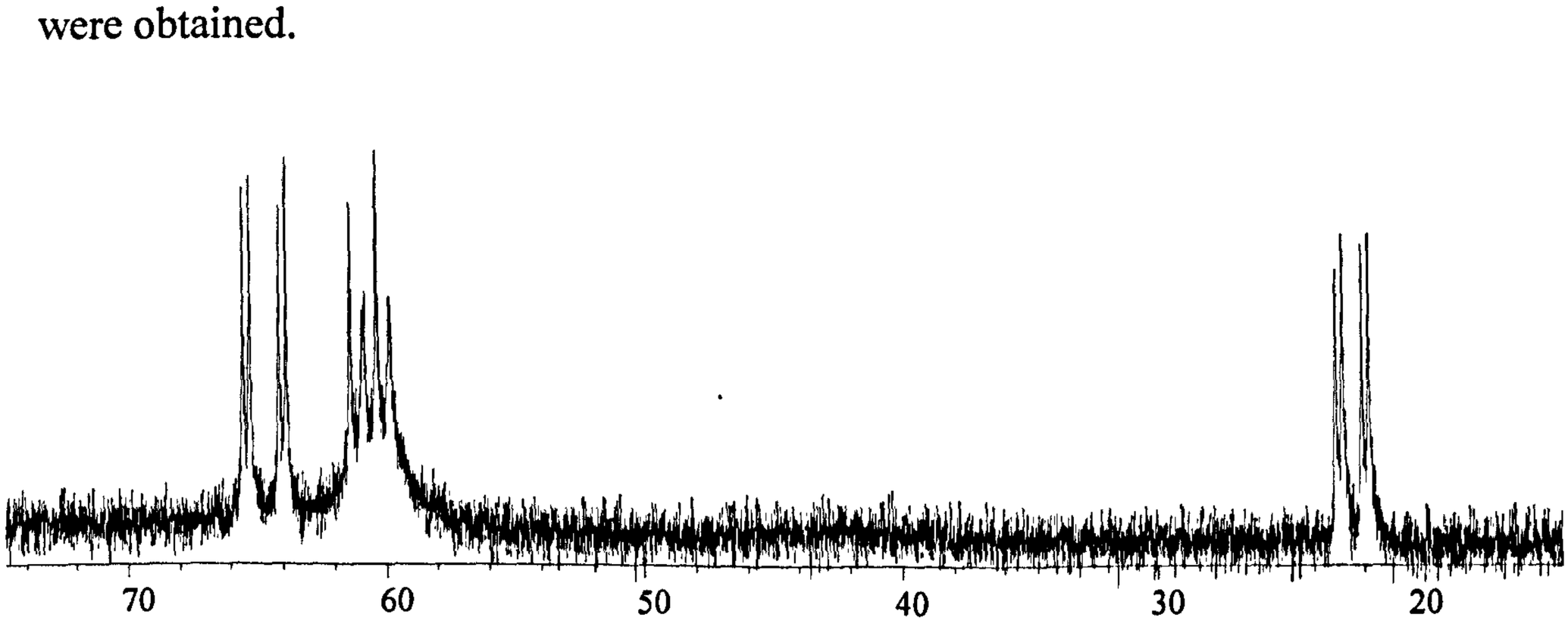


Figure 5-15: $^{31}P\{^1H\}$ spectrum of $[RhCl(CO)_2]_2$ and DTBPMB under CO in d^2-DCM

In order the confirm the presence of $[RhCl(DTBPMB)]_2$ its synthesis was attempted using the following procedures: $[RhCl_3 \cdot 3H_2O]$/DTBPMB in methanol, $[RhCl(cot)_2]_2$/DTBPMB in DCM and $[RhCl(cod)_2]_2$/DTBPMB in both methanol and DCM. All these attempts to prepare the desired dimer failed. However, an unexpected product was obtained when $[RhCl(cod)_2]_2$ and DTBPMB were refluxed in methanol (*Illustration 5- 4*). The two chlorine bridges in the initial

rhodium complex were broken and one molecule of phosphine formed a new bridge between the two rhodium atoms. As far as we are aware this is the first metal compound which has a bridging DTBPMB ligand. This crystal structure is discussed in section 5.3.4.

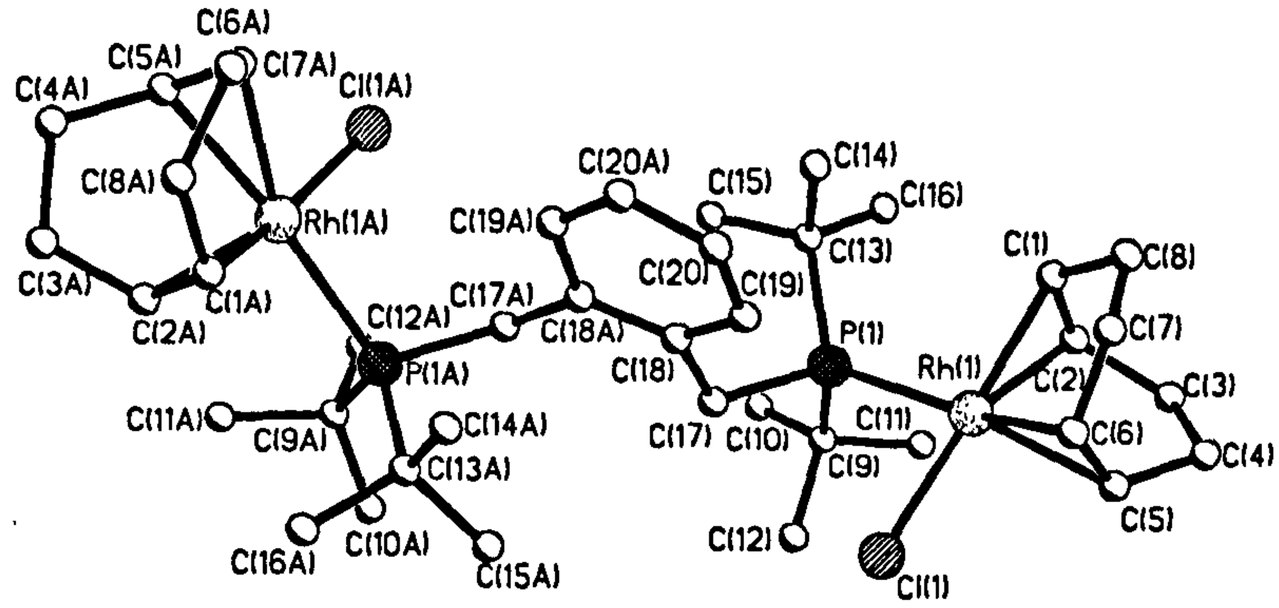


Illustration 5- 4: Crystal structure of $[Rh_2Cl_2(\mu^1\text{-DTBPMB})(cod)_2]$

5.3.3.4. Reaction of $[RhCl(CO)_2]_2$ with DTBPMB in methanol

$[RhCl(CO)_2]_2$ and DTBPMB were dissolved in d^4-MeOH under argon. The solution was introduced under inert atmosphere into the HPNMR cell, which was pressurised with 15 bar of CO. The ^{31}P NMR spectrum (*Figure 5-16*) showed one doublet at 38.9 ppm (J_{Rh-P}= 124.8 Hz) assigned to the complex $[Rh(DTBPMB)Cl(CO)_2]$. In order to confirm that the complex contained two CO ligands, the experiment was run under labelled carbon monoxide (^{13}CO). The spectrum recorded under ^{13}CO showed a complex pattern simulated (*Figure 5-16*) as arising from the A part of an AA'XX'M/ AA'XM spin system. Two different spin systems were observed due to the presence of molecules containing two ^{13}CO (AA'XX'M) and molecules containing just one ^{13}CO (AA'XM) in the solution. For simplicity both spin systems were simulated ignoring the splitting of the lines due to the presence of the metal (M). Thus, the AA'XX' part of the spectrum was

simulated using the following parameters: $J_{AA'}$= 30 Hz, $J_{XX'}$= 10 Hz, J_{AX}= 89 Hz, $J_{AX'}$= -20 Hz (black spectrum in *Figure 5-17*) and the AA'X part of the spectrum was simulated using the following parameters: $J_{AA'}$= 30 Hz, J_{AX}= 89 Hz, J_{AX}= -20 Hz (red spectrum in *Figure 5-17*).

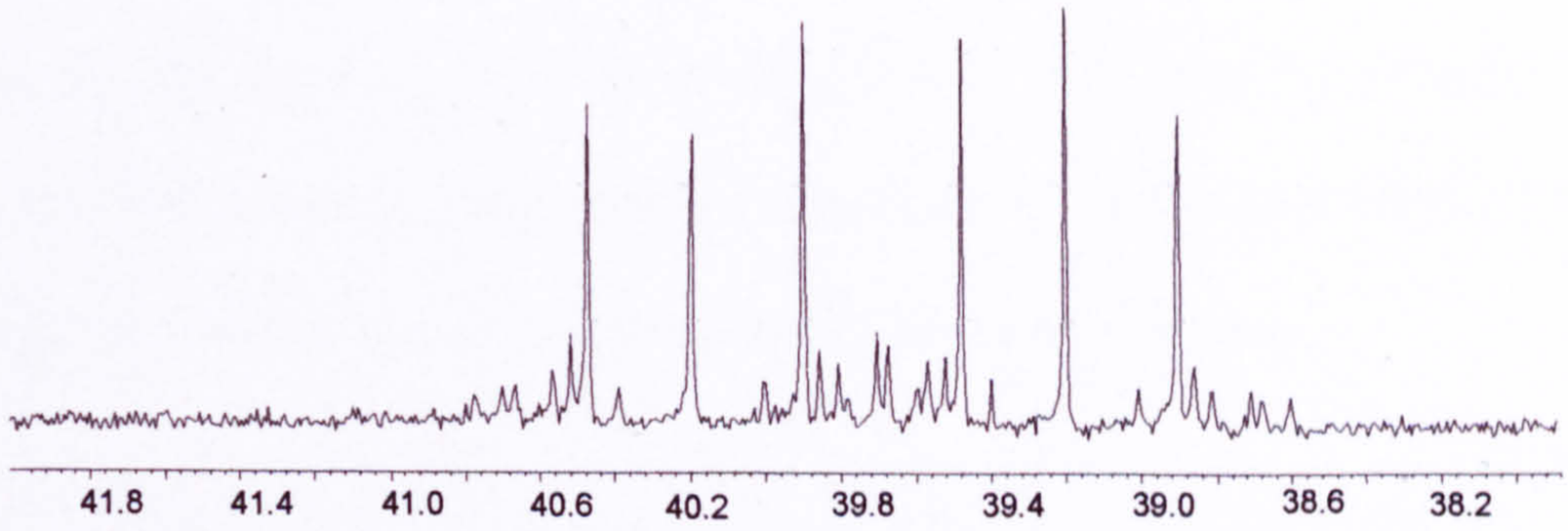


Figure 5-16: $^{31}P\{^{d}H\}$ spectrum of $[RhCl(CO)_2]_2$ and DTBPMB under ^{13}CO in d^4-MeOH

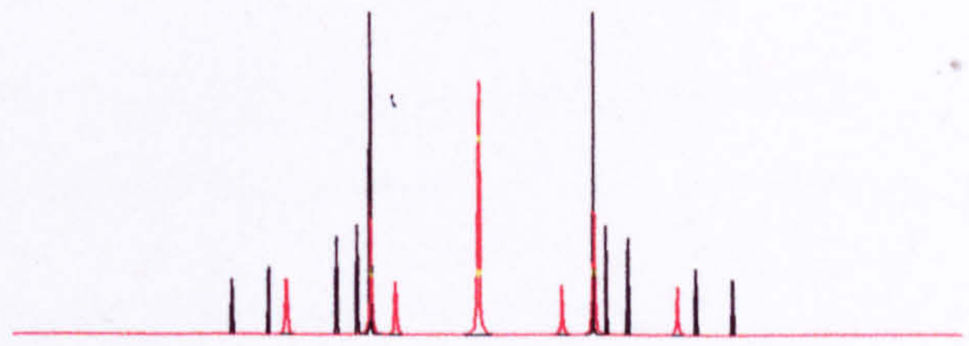


Figure 5-17: Simulated spectrum for overlapped AA'XX' and AA'X spin systems

This spectrum is consistent with a reaction between [Rh(DTBPMB)Cl(CO)] and ^{13}CO leading to [Rh(DTBPMB)Cl($^{13}CO)_2$] in an irreversible reaction at temperatures in the range 20-100 °C. Thus, the coordinated CO does not exchange rapidly with free CO on the NMR scale. The possible structures for the dicarbonyl which have equivalent phosphorus and equivalent CO are shown in Figure 5-18. Structure a, however, would exhibit an A_2X_2M spin system (doublets of triplets in both the ^{13}C and ^{31}P NMR spectra of [Rh(DTBPMB)Cl($^{13}CO)_2$].

Structure b has mutually cis P atoms and the two C atoms are almost trans to each of the P atoms in the basal plane of a square pyramidal complex. The observed coupling constants (J_{PP}= 30 Hz, $J_{P\text{-}C(cis)}$= -20 Hz, $J_{P\text{-}C(trans)}$= 89 Hz) suggest that the

relative position of the carbon and the phosphorus is trans to one another and therefore structure b seems to be the most likely. The coupling constants used for the simulation of both spins systems are also consistent with the formation of a slightly bent square pyramidal [Rh(DTBPMB)Cl($^{13}CO)_2$]. This structure has been reported to be also possible for [RhCl$(CO)_2(PEt_3)_2$][13] and [RhI$(CO)_2(PEt_3)_2$][10]. However, for both complexes the structure suggested to be the most likely was that in which the two CO ligands and the two PEt_3 are mutually trans.

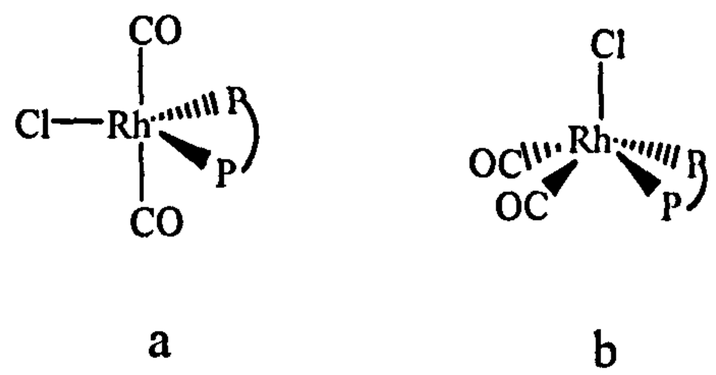


Figure 5-18: Possible structures for the reaction of [RhCl$(CO)_2]_2$, DTBPMB and CO

We note that the chemical equivalence of the two carbon atoms and the two phosphorus atoms cannot arise because of fluxionality as this would render each pair of atoms magnetically equivalent also.

5.3.4. Crystal structure analysis

Crystal structures of [Rh(DTBPMB)X(CO)], X= Cl, I, were obtained.

Table 5- 1 and Table 5- 2 show selected bond lengths and angles for each complex and they are defined in *Figure 5-19*.

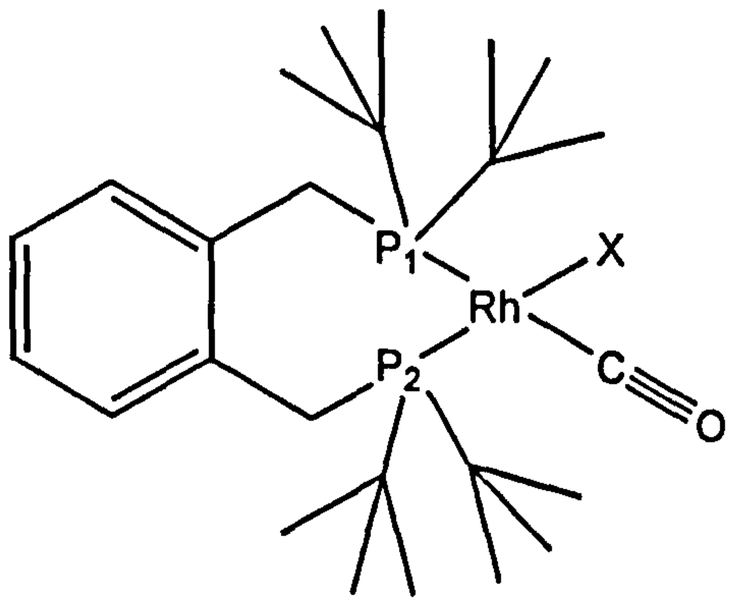


Figure 5-19: Definition of the bond lengths and angles

Table 5- 1: Selected bond lengths for complexes [Rh(DTBPMB)XCO)], X= Cl or I

Complex	Rh-P_1 (A)	Rh-X (A)	Rh-C (A)	Rh-P_2 (A)	C-O (A)
[Rh(DTBPMB)Cl(CO)]	2.404	2.499	1.936	2.285	0.936
[Rh(DTBPMB)I(CO)]	2.443	2.721	1.847	2.292	1.125

Table 5- 2: Selected bond angles for complexes [Rh(DTBPMB)XCO)], X= Cl or I

Complex	P_1-Rh-X (°)	X-Rh-C (°)	C-Rh-P_2 (°)	P_1-Rh-P_2 (°)
[Rh(DTBPMB)Cl(CO)]	92	81.4	89.5	101.2
[Rh(DTBPMB)I(CO)]	95	78.6	89.9	100.2

Both complexes have similar Rh-P_1 and Rh-P_2 distances. However, the Rh-X, Rh-C and C-O differ significantly. The Rh-Cl is considerably shorter than the Rh-I bond due to the larger radius of I compared to that of Cl. Because of the higher electronegativity of Cl, the Cl atom withdraws electron density from the metal centre very effectively making it less electron rich and therefore the back donation to the * orbital of the carbonyl is lower. This makes the Rh-C shorter and the C-O longer than in the case of I.

The P_1-Rh-P_2 angle and P_2-Rh-C angle are comparable in both structures (~100° and ~89°, respectively). However, the P_1-Rh-X angle is larger for I (95°) than for Cl (92°), probably due to the steric hindrance encountered from the tert-butyl groups. Thus, the X-Rh-C angle is forced to be smaller when X= I (78.6°) than when X= Cl (81.4°).

A slightly shorter Rh-Cl bond was found for the complex [(DTBPMB)$Rh_2Cl_2(cod)_2$] (Rh-Cl= 2.396 Å) compared to that for [Rh(DTBPMB)Cl(CO)] (Rh-Cl= 2.499 Å). However, the Rh-P distance found for [(DTBPMB)$Rh_2Cl_2(cod)_2$] (Rh-P= 2.422 Å) was very similar to that found for the phosphorus cis to the chloride in [Rh(DTBPMB)Cl(CO)] (Rh-P= 2.404 Å) and considerably longer than that for the phosphorus trans to chloride (Rh-P= 1.936

Å). In addition the Cl-Rh-P angle is smaller for the dimer (89.33 °) than for [Rh(DTBPMB)Cl(CO)] (92 °).

5.4. Conclusions

The catalytic system based on $[RhCl(CO)_2]_2$-DTBPMB gives higher initial rates than the Monsanto catalyst under 150 °C and 180 °C for the carbonylation of methanol. Detailed HPIR and HPNMR studies carried out showed that, unfortunately, the active species is not stable under reaction conditions decomposing to the monoanion $[Rh(CO)_2I_2]^-$ (Monsanto catalyst), which is a less efficient catalyst, and the quaternary phosphonium salt. Thus, the higher rate observed in the presence of DTBPMB may be due to the promoting effect of inorganic iodide. The mixture [Rh(DTBPMB)(I)(CO)] and iodide is active for this process. Hence, to increase the rate of carbonylation, iodide must be facilitating the reaction between them to afford the active Monsanto species and the phosphonium salt. The decrease on the water concentration from 17 % w/w to 3 % w/w led to an extremely slow reaction.

There is some tension between the results obtained using HPIR and HPNMR since signals apparently from $[Rh(DTBPMB)(CO)MeI_2]$ and [Rh(DTBPMB)(COMe)(CO)Me] are observed in the IR spectrum but not in the ^{31}P NMR spectra. The main differences between these experiments are the concentration of rhodium precursor and the lack of stirring in the HPNMR experiments.

5.5. References

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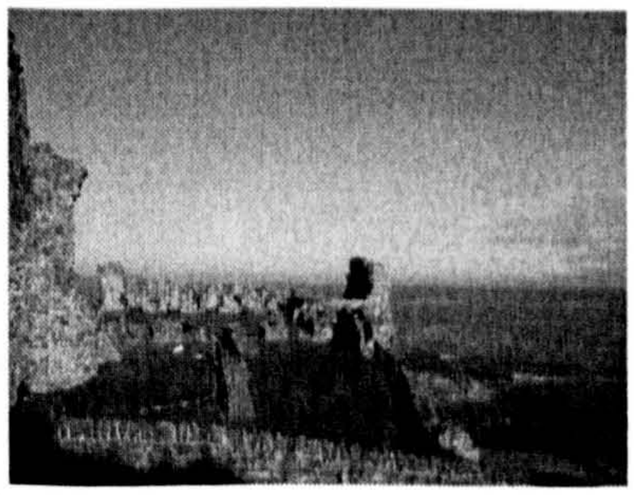
Chapter 6:

CONCLUSIONS

AND FUTURE WORK



6.1. Conclusions and future work

In conclusion we have shown that Pd complexes of the Lucite International ligand (DTBPMB) are highly active for the methoxycarbonylation of a variety of alkenes and show very high selectivity towards the production of linear esters under mild conditions of temperature and pressure (room temperature, 1 bar of carbon monoxide).

The selectivities towards the desired linear product are the highest reported for alkoxycarbonylation reactions, > 99 % for terminal alkenes (C_8-C_{12}). Internal alkenes could also be carbonylated giving very high selectivities (> 99%) to terminal esters. This is important because alkenes are often available as mixtures with the double bond in a variety of positions.

Almost complete conversion was achieved when the reaction was carried out in alcohols other than methanol. The corresponding linear ester was produced with 97-99 % selectivity depending upon the bulkiness and the nucleophilic character of the alcohols.

Either terminal or internal branched pentenes underwent carbonylation of the terminal position. A remarkable result was obtained when 2-methyl-1-pentene was the substrate. The rate of isomerisation could be controlled by the availability of carbon monoxide, being higher when the gas was less available. Hence, the least hindered terminal position (carbon 5) is preferentially carbonylated over the other extreme of the chain (carbon 1) when the CO availability is low.

Functionalised alkenes have been also successfully methoxycarbonylated. Not only is the reactivity of the internal or terminal double bond unaffected by the presence of groups like COOMe, CN or COOH, but also the conjugation between

two double bonds could be broken leading to a difunctionalised saturated chain, although with carbonylation of the terminal carbon atom.

Likewise, vinyl groups attached to a silicon atom have been carbonylated towards the linear ester. However, allyl alcohol did not undergo methoxycarbonylation, probably because a five membered ring is formed in the course of the catalytic cycle.

Carboxylic acids can also be produced when H_2O is used instead of an alcohol. Nonanoic acid was produced from 1-octene, CO and water. Although the conversions obtained were lower than for the methoxycarbonylation reaction, the selectivity to linear carboxylic acid achieved was higher than 97 %.

Ligands which contain isobutyl, cyclopentyl and phenyl groups instead of tert-butyl groups attached to the phosphorous atoms turned out to be unsuitable for carbonylation reactions.

Catalytic results obtained for the methoxycarbonylation of linear alkenes were highly satisfactory. However, the use of this catalytic system in ionic liquids-supercritical CO_2 was unsuccessful due to the extraction of the neutral species [Pd(DTBPMB)(CO)]. Thus, the synthesis of an ionic derivative of the ligand is required to attempt the methoxycarbonylation reaction under these conditions. In addition, spectroscopic studies under reaction conditions (room temperature and low CO pressure) and under more severe conditions would provide information regarding the species involved in the catalytic cycle. Preliminary studies show that many complexes and uncharacterised species may be present.

The *in situ* catalytic system formed by $PdCl_2$-DTBPMB in ether under CO at 100 °C leads to the selective formation of amides from linear terminal or internal

alkenes and aromatic amines. However, if the reaction is carried out in THF, the product obtained is N-phenyl-pyrrolidine. High pressure NMR studies could provide evidence concerning the mechanism operating in the formation of this product. This reaction has been shown to be general, with many 5-membered rings containing oxygen being transferred into the analogous cyclic amine (amide).

Selective carbonylation of aryl chlorides to esters is catalysed by Pd/BDTBPMB complexes in alcohols in the presence of base. In many cases the reaction produced a difficult to separate mixture of compounds.

For moderately activated aromatic rings, like 4-chloroacetophenone, selective carbonylation can only be achieved when weak nucleophile alcohols such as 2,2,2-trifluoroethanol are used. Stronger nucleophilic alcohols give many side products arising from nucleophilic aromatic substitution, H for Cl exchange and an unusual transformation of the methylketone into a methyl ester. Labelling studies show that this reaction formally occurs by displacement of the methyl group by methoxide.

The role of the base used has also been investigated. Common organic and inorganic bases of different strength have been used for this purpose. The presence of a weak base like triethylamine did not allow the reaction to proceed fast, however, the selectivity achieved was higher. Strong bases like $KOBu^t$ speeded up the reaction, but a mixture of products was formed.

High selectivity towards the carbonylation product was achieved when the reaction was carried out in TFE or 1-propanol. However, the dimethyl ester was produced when methanol was the solvent. Mechanistic studies under reaction

conditions (HPNMR and HPIR) are required to understand the displacement of the methyl group by methoxide.

We have carried out a detailed study of hydroformylation reaction of terminal alkenes and allyl alcohol and some work on vinyl acetate. This study has focused on the catalytic activity of different rhodium complexes modified by 1,2-bis(dialkylphosphinomethyl)benzene/ bis(diphenylphosphinomethyl)benzene type ligands.

Hydroformylation of 1-hexene was carried out using $[RhCl(CO)_2]_2$, $[Rh(acac)(CO)_2]$, $[Rh(OAc)_2]_2$ and $[RhCl_3{\cdot}3H_2O]$ as the rhodium precursors. High activity and acceptably selectivity towards the linear aldehyde were achieved when $[RhCl(CO)_2]_2$, $[Rh(acac)(CO)_2]$ or $[Rh(OAc)_2]_2$ were modified by DTBPMB.

Hydroformylation of 1-octene was carried out using $[RhCl(cod)_2]_2$ and $[RhCl(cot)_2]_2$ in addition to the previously mentioned rhodium precursors. The *in situ* formed Rh/DTBPMB catalysts gave excellent conversion and moderate selectivity to aldehydes in all cases, except for $[RhCl(cot)_2]_2$, which was highly uneffective.

The use of DIBPMB, DPhPMB and DCypPMB as the ligands led to active catalytic systems. However, the conversions and selectivities obtained were lower than those obtained with DTBPMB. We found that the catalyst gave higher selectivity to aldehydes under a higher partial pressure of CO. However, lower linear selectivity was achieved, suggesting that both the linear and the branched Rh-alkyl are rapidly trapped by CO.

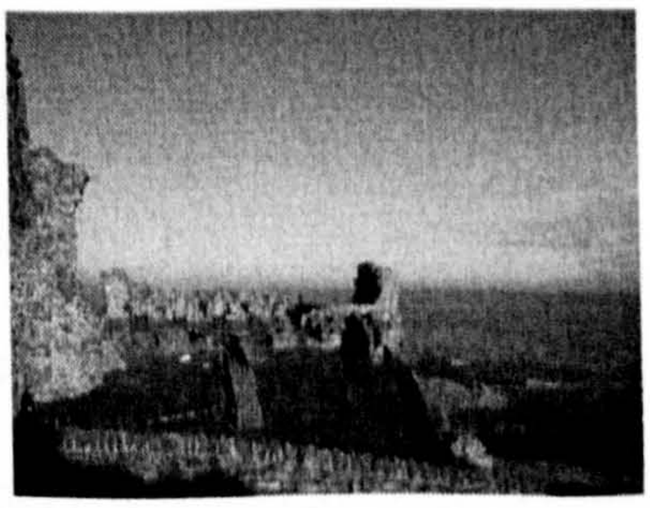
A great improvement was achieved when chlorine was present in the solution, either in the solvent (DCM) or by using a chlorine containing rhodium precursor. The catalytic systems formed by $[RhCl(CO)_2]_2$/DTBPMB in toluene and $[Rh(acac)(CO)_2]$/DTBPMB in DCM were the most effective. The better results obtained in the presence of chlorine are rationalised on the basis of a partial inhibition of the hydroformylation of isomerised alkenes, which led to higher linear selectivity than when chlorine was absent.

No mechanistic studies were carried out on this reaction. Labelling studies in deuteriated dichloromethane would give a clearer indication on how it enters the catalytic cycle and its role in the catalytic cycle. The presence of other halogens could also be studied.

The catalytic system formed *in situ* from $[RhCl(CO)_2]_2$-DTBPMB-MeI is unstable under the reaction conditions required for the methanol carbonylation. The rhodium complex formed with the diphosphine in first instance decomposes to the more stable Monsanto catalyst and the phosphonium salt derived from the diphosphine. The higher rates obtained in the presence of DTBPMB compared to those obtained in the absence of diphosphine is tentatively attributed to the higher concentration of inorganic iodide in the reaction mixture.

Chapter 7:

EXPERIMENTAL



7.1. Experimental.

All experiments atmosphere were carried out under a dry argon on vacuum line using standard Schlenk line and catheter tubing techniques. Argon was dried through a Cr (II) / silica packed glass column. Liquids were transferred under inert atmosphere by syringe or cannula through suba seals. Solids were transferred directly from one Schlenk tube to another or weighed out in a glove box under argon.

All gases were purchased from BOC gases. Ethanol and methanol were distilled over magnesium alkoxide under nitrogen and stored under nitrogen over molecular sieves. Toluene, tetrahydrofuran and hexane were stored over sodium. Petroleum ether and diethyl ether were distilled over sodium diphenylketyl. Dichloromethane was distilled over calcium hydride. Anisole was degassed by bubbling argon through the syringe. Ethylene glycol (Avocado) and triethylene glycol (Aldrich) were degassed by bubbling nitrogen. Deuteriated solvents were purchased from Cambridge Isotope Laboratories, degassed by bubbling argon through them and stored under argon over molecular sieves.

The metal complexes $[Pd_2(dba)_3]$ (Aldrich), $[PdCl_2]$ (Lancaster), $[RhCl(CO)_2]_2$, $[Rh_2(OAc)_4]$, $[RhCl_3{\cdot}3H_2O]$, $[Rh(CO)_2(acac)]$ (Strem) were stored in a glove box under argon atmosphere. The diphosphine 1,2-bis(di-tert-butylphosphinomethyl)benzene (Lucite International) was stored and handled in a glove box.

The substrates 1-octene, 2-octene, 3-octene, 4-octene, 1-hexene, 1-dodecene (Aldrich) were purified by distillation and degassed by bubbling argon. 1,3-butadiene (BOC gases or Aldrich) was used as received. Styrene (Aldrich) was degassed by bubbling argon. Allyl alcohol (Lancaster) was stored under argon

over molecular sieves in the dark. The aryl chlorides 4-chloroacetophenone (Lancaster), 4-chloromethylbenzoate (Aldrich), 1,4-dichlorobenzene (Aldrich), 4-chloroanisole (Aldrich), 2-chloromethylbenzoate (Aldrich), acetophenone (Aldrich), 4-chlorobenzonitrile (Aldrich) and nitrobenzene (Aldrich) were used as received. The amines aniline, *o*-, *m*-, *p*-aminotoluene, *m*-, *p*-chloroaniline, *o*-amino-methyl benzoate and *m*-, *p*- amino-benzoic acid were used as received. Methanesulfonic acid (Aldrich) was dried over molecular sieves. The bases, sodium acetate (Aldrich), KOH (Aldrich) and triethylamine (Avocado), were used in air as received, whereas potassium *tert*-butoxide (Lancaster) was stored in a glove box.

7.2. Analytical Techniques.

Infrared spectra were obtained using a Nicolet Protege 460 Fourier Transform Spectrometer with CsI optics. The infrared spectrometer was interfaced to a personal computer via the OMNIC operating system.

G.C. analysis were carried out using a Hewlett-Packard 5890 series gas chromatograph equipped with a flame ionisation detector for quantitative analyses and a Hewlett-Packard 5890 series mass selective detector fitted with a SUPELCO MDN-35 35 % phenyl/ 65 % methyl-polysiloxane capillary column for qualitative analyses by G.C.M.S. The temperature programme used was: 50 °C (4 minutes), Δ 20 °C/ minute to 130 °C (2 minutes), Δ 20 °C/ minute to 220 °C (15.5 minutes). Helium was used as the carrier gas with an initial flow of 1 ml/ minute.

^{13}C, ^{1}H and ^{31}P NMR spectra were recorded on a Bruker AM 300 NMR spectrometer or a Varian 300 NMR spectrometer. Broad band decoupling was

used for ^{13}C spectra and ^{31}P spectra. ^{1}H and ^{13}C NMR spectra were referenced internally to deuterated solvents, which were referenced relative to TMS at δ=0: CD_2Cl_2: ^{1}H, δ, 5.35 ppm, ^{13}C, δ, 53.8 ppm; CD_3OD: ^{1}H, δ, 3.35 ppm, ^{13}C, δ, 49.0 ppm; C_6D_6: ^{1}H, δ, 7.16 ppm, ^{13}C, δ, 128.39 ppm; C_7H_8: ^{1}H, δ, 2.09 ppm, ^{13}C, δ, 20.4 ppm; $CDCl_3$: ^{1}H, δ, 7.27 ppm, ^{13}C, δ, 77.23 ppm. ^{31}P NMR spectra were referenced externally to 85 % H_3PO_4. Coupling constants are given in Hz.

7.3. Preparation of solutions for catalyst testing.

7.3.1. Methoxycarbonylation of alkenes.

All the catalytic solutions were made up as follows: $Pd_2(dba)_3$ (45.7 mg, 0.05mmol) and DTBPMB (depending on the experiment) were weighed into a Schlenk tube in a glove box. Methanol (10 cm^3) was then added with a syringe and the solution was warmed with a heat gun to dissolve all the solids. When the tube was cooled, substrate (2 cm^3) and methanesulphonic acid (MSA) (65 μl, 0.01 mmol) were added. The solution was then transferred to a degassed autoclave made of hastelloy, which contained a magnetic stirrer, and had been previously cleaned with acid, water and acetone and dried in an oven. The whole system was flushed three times with CO and then pressurised. It was heated at 80 °C for 3-16 hours and then cooled in air and vented.

When the substrate was butadiene the solution preparation was different. The catalysts solutions were transferred *via* cannula to the previously degassed autoclave, which was then attached to the 1, 3-butadiene cylinder and charged with 1.8-4 bar. Liquid 1, 3-butadiene was obtained by transferring it to a stainless steel container cooled to -78 °C with liquid nitrogen. The volume of 1, 3-butadiene was measured by transferring it to a graduated flask, which was then

attached to the autoclave. The autoclave was pressurised with CO, heated at 50-120 °C for 6-24 hours, cooled and slowly vented.

The experiments under 1 bar of CO and at room temperature were carried out in a dried a degassed Schlenk flask. The catalytic solutions were made up in the same way and the CO was bubbled through the solution exiting through a needle in a subaseal.

In all cases the yellow solution obtained was analysed by GCFID. Conversion, selectivity and l: b ratio were calculated as follows:

Conv=100-[(total area of alkenes/total area) x 100]

Selec= % linear ester/ conv

l:b= % linear ester/ % all branched ester

To calculate the conversion of 1,3-butadiene the GC equipment was calibrated as follows. Solutions of known concentrations of dimethyl adipate and 3-methylpentenoate were prepared. The areas were plotted against the concentrations to obtain a calibration graph from which the concentration of the products, and therefore the number of moles of each product, could be calculated. As the initial number of moles was also known, the yields were obtained as follows: [(moles of product/ moles of butadiene) x 100].

7.3.2. Aminocarbonylation of alkenes.

[$PdCl_2$] (32 mg, 0.1 mmol) was placed in the autoclave, which was then flushed 3 times with CO. DTBPMB (50 mg, 0.25 mmol) was dissolved in diethyl ether (10 ml) in a degassed Schlenk. 1-octene (1 ml, 6 mmol) and the amine (11 mmol) were then added to that solution, which was transferred to the autoclave via

cannula. The autoclave was pressurised with 20 bar of CO and heated to 100 °C for 3-6 h, cooled and vented. The recovered solution was analysed by GCFID.

7.3.3. Methoxycarbonylation of aryl chlorides.

The catalytic solutions were made up as follows: $PdCl_2$ (32 mg, 0.1 mmol), DTBPMB (100 mg, 0.5 mmol) and KO^{t}Bu (800 mg, 8 mmol) were weighed into a Schlenk tube in a glove box. Methanol (10 cm^3) was added with a syringe and the solution was warmed with a heat gun to dissolve all the solids. When the base used was NaOAc (8 mmol), KOH (8 mmol) or NEt_3 (8 mmol) they were added after the methanol. Once all the solids were dissolved, the substrate (8mmol) was added. The solution was then transferred via cannula to a dry and degassed hastelloy autoclave, which was pressurised with 20 bar of CO and heated at 100 °C for 24-48 h, cooled and vented. The solutions were analysed by GCFID.

7.3.4. Hydroformylation of alkenes.

All the catalytic solutions were made up as follows: $[RhCl(CO)_2]_2$, $[Rh_2(OAc)_4]$, $[RhCl_3{\cdot}H_2O]$ or $[Rh(acac)(CO)_2]$ (0.023 mmol) and DTBPMB (20 mg, 0.046 mmol) were weighed into a Schlenk tube in a glove box. The solvent, toluene, tetrahydrofuran, DCM, MeOH, ^{t}BuOH or OctMiMTfN (10 ml), was added with a syringe. When all the solids were dissolved, the substrate (1-octene, 1-hexene or allyl alcohol) (2 ml) was added to the solution. The dry degassed hastelloy autoclave was flushed three times with argon. The catalytic mixture was transferred to the autoclave via cannula. The autoclave was pressurised with synthesis gas and heated for 3 hours, cooled and vented. The solutions were analysed by GCFID.

The outcome of these experiments is expressed in terms of conversion of the starting material, selectivity to aldehydes and selectivity to linear aldehyde. These magnitudes are defined as follows:

Conv= 100 - % 1-alkene.

S ald= [% aldehydes/ conv] x 100

S linear= [% linear aldehyde/ % aldehydes] x 100

7.3.5. Methanol carbonylation.

The autoclave was charged in a glove box with the catalyst. A solution containing methyl acetate (6 ml), acetic acid (2 ml) and water (1 ml) was added to the thoroughly carbon monoxide flushed autoclave, which was flushed three times with approximately 30 bar of carbon monoxide and finally pressurised to 10 bar. The autoclave was heated to 150 °C, the pressure in the autoclave was raised to 27 bar and the temperature allowed to stabilise. Methyl iodide (1 ml) was added to the solution via the catalyst injector to initiate the reaction.

7.3.6. Preparation of catalytic solutions to be run in a constant pressure kinetics.

A schematic of the CATS kinetic autoclave can be seen in *Figure 6-1*. The set-up includes an autoclave (A), an injection arm (B), a pressure controller and transducer (C), a ballast vessel (D), and a control panel (E). Each section can be isolated from the others with valves.

The reaction took place in the autoclave, which was flushed with CO and H_2. The catalyst solution was injected with a gas tight syringe. The autoclave was then closed and heated to the reaction temperature and pressurised to just below the

reaction pressure. The substrate was then injected with a stream of synthesis gas which brought the autoclave to the reaction pressure. As the reaction proceeded the synthesis gas was consumed. The pressure in the autoclave, however, was kept constant by the pressure controller, the gas stream was fed by the ballast vessel which was pressurised to a value such that when the reaction was over it would still be higher than the pressure in the reaction vessel. There are gas inlets to the autoclave and ballast vessel, which allows for them to be filled with gas independently of each other. The pressures of the autoclave, ballast vessel, and injection port were monitored by pressure transducers, which were in turn controlled from the control panel.

The gas consumed by the reaction was monitored by recording the drop in pressure in the ballast vessel during the reaction period. Data were collected via a link from data logging hardware (Pico Monitor, model ADC16) which was fitted to a PC though a COM port. The computer used data logging software (PicoLog for Windows, version 5.04.2) to monitor and record the pressures. The data collected then allowed for the calculation of the rates of reaction.

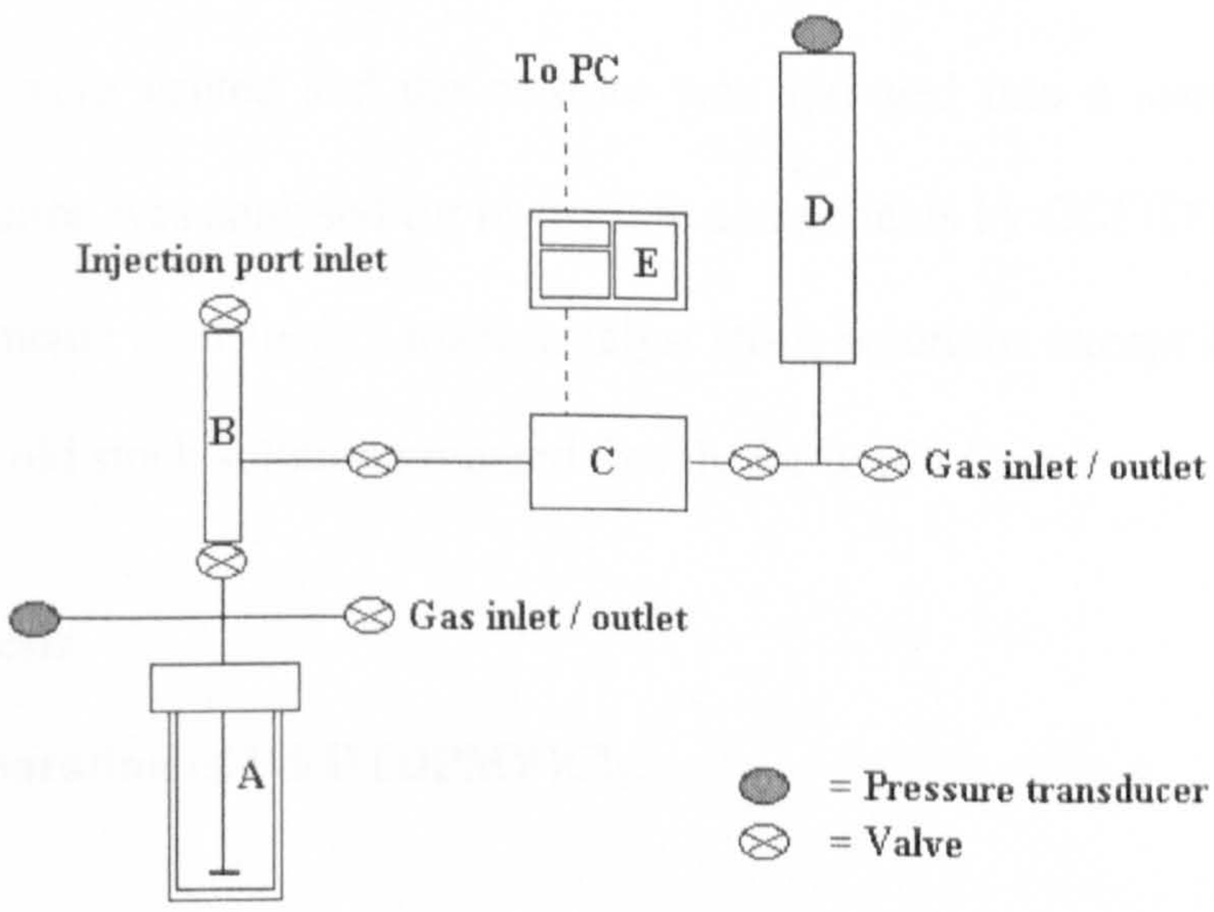


Figure 6- 1: ***Schematic of the CATS kinetic autoclave.***

Typical Run (Expt 6, Table 2-19): an autoclave, fitted with a substrate injector containing 1-octene (2 ml, 12.74 mmol), a mechanical stirrer, a gas delivery system, an injection port and a thermocouple was flushed with CO to remove air. A deep red methanol (6 ml) solution containing $Pd_2(dba)_3$ (0.0183g, 0.040 mmol Pd), DTBPMB (0.0474g, 0.120 mmol) and methane sulphonic acid (6µl, 0.093 mmol) was added through the injection port against a stream of CO using a syringe. These quantities afford a [Pd] of 5 mmol l^{-1} and a Pd: ligand: MSA: 1-octene ratio of 1: 3: 2.3: 319. The autoclave was pressurised with CO to 20 bar and the pressure released. This flushing procedure was repeated twice more. After pressurising to 24 bar the stirrer was started (1000 rpm) and the autoclave was heated to 100°C for 45 mins. The 1-octene was then added to the autoclave by forcing it in through the substrate injector using a CO pressure of 30 bar. The temperature, pressure in the autoclave and pressure in a ballast vessel, from which gas was fed into the autoclave through a mass flow controller to keep the pressure within the autoclave constant at 30 bar, were monitored and recorded every 5 seconds. After 6 hours the autoclave was cooled in water and the stirrer stopped. The gases were vented and the mixture was syringed into a sample vial. The yellow solution was analysed for its organic components by GCFID and GCMS. All experiments used freshly made catalyst stock solutions except Expt 8, which used 1 day old stock solution prepared freshly for use in Expt 7.

7.4. Synthesis

7.4.1. Preparation of $Pd(DTBPMB)Cl_2$.

A solution of 1,2-bis-(di-*tert*-butylphospinomethyl)benzene (39.4 mg, 0.1 mmol) in methanol was added via syringe to a solution of sodium tetrachloropalladate

(14.7 mg, 0.05 mmol) in methanol (10 cm^3) and the solution stirred overnight at room temperature. The resultant yellow precipitate was filtered via cannula, washed with ethanol and recrystallised from DCM/ MeOH to yield orange crystals (40 mg, 70%), $^{31}P\{^1H\}$: δ_P=35.4 (s). This complex was prepared by Eastham in 2002 (δ_P=35.0 (s)).[1]

7.4.2. Preparation of [Rh(DTBPMB)Cl(CO)]

$[RhCl(CO)_2]_2$ (40 mg, 0.1 mmol) and DTBPMB (80 mg, 0.2 mmol) were dissolved in DCM (10 ml) under argon. The complex [Rh(DTBPMB)Cl(CO)] was formed almost instantaneously at room temperature. The yellow solid was filtered, washed with DCM and recrystallised from diethyl ether at low temperature to yield yellow crystals (47 mg, 84 %). $^{31}P\{^1H\}$: δ_P= 63 ppm (dd), 23 ppm (dd). IR: γ_{CO}= 1945 cm^{-1}. Anal. Calcd for $C_{25}H_{44}ClP_2ORh$: C, 53.53 %, H, 7.91 %. Found: C, 53.8 %, H, 8.33 %

7.4.3. Preparation of [Rh(DTBPMB)Cl(CO)$_2$]

$[RhCl(CO)_2]_2$ (20 mg, 0.05 mmol) and DTBPMB (40 mg, 0.1 mmol) were dissolved in methanol (3 ml) under argon. A yellow solid precipitated instantaneously (23 mg, 80 %). Attempts of recrystallisation were unsuccessful due to the insolubility of this solid. δ_P= 38.6 ppm (J_{Rh-P}= 121 Hz). δ_C= 40 ppm

$[RhCl(CO)_2]_2$ (20 mg, 0.05 mmol) and DTBPMB (40 mg, 0.1 mmol) were dissolved in DCM (3 ml) under argon. The solution was introduced via cannula in the high pressure NMR cell, which was pressurised with 20 bar of CO and placed in the spectrometer. The recovered solution contained a yellow precipitate which

was very insoluble in common organic solvents. $^{31}P\{^{1}H\}$: δ_P= 40 ppm, ^{13}C: δ_C= 40 ppm. IR: γ_{CO}= 1938 cm^{-1}, γ_{Rh-Cl}= 226 cm^{-1}.

7.4.4. Preparation of [Rh(DTBPMB)I(CO)]

$[RhCl(CO)_2]_2$ (40 mg, 0.1 mmol) and DTBPMB (80 mg, 0.2 mmol) were dissolved in DCM (8 ml) under argon. Methyl iodide (2 ml) was added to the solution, which was stirred overnight at room temperature. The resultant orange precipitate was filtered, washed with DCM and recrystallised from diethyl ether at low temperature (57 mg, 88 %). $^{31}P\{^{1}H\}$: δ_P= 60 ppm (dd), 27 ppm (dd). IR: γ_{CO}= 1945 cm^{-1}. Anal. Calcd for $C_{25}H_{44}IP_2ORh$: C, 46.03 %, H, 6.80 %. Found: C, 46.45 %, H, 7.13 %

7.4.5. Preparation of [Rh(DTBPMB)(cod)$_2$Cl$_2$]

$[RhCl(cod)_2]_2$ (18 mg, 0.025 mmol) and DTBPMB (20 mg, 0.05 mmol) were dissolved in methanol (10 ml) under argon. The solution was refluxed at 55 °C for 2 hours. Green crystals precipitated once the mixture was allowed to cool to room temperature. The crystals were filtered, washed with methanol and recrystallised from methanol at room temperature (9 mg, 73 %). $^{31}P\{^{1}H\}$: δ_P= 77 ppm (dd). Anal. Calcd for $C_{40}H_{68}Cl_2P_2Rh_2$: C, 54.00 %, H, 7.93 %. Found: C, 54.37 %, H, 8.31 %

7.4.6. Preparation of [(DTBPMB)Me]$^+$I$_3$

Following the procedure for the preparation of the solution for the methanol carbonylation reactions described in section 7.3.5, dark red crystals were formed

at room temperature with time. $^{31}P\{^{1}H\}$: δ_P= 50 ppm (s). Anal. Calcd for $C_{26}H_{50}I_6P_2$: C, 26.33 %, H, 4.25 %. Found: C, 26.52 %, H, 4.48 %

7.5. HPNMR

The high pressure NMR equipment consists of a sapphire and titanium cell, a brass and aluminium housing, two brass fittings, an NMR spinner, a spiral hose, and an extendable clamp. The sapphire titanium cell has been pressure tested to 100 bar and 100 °C, although the specifications are greater than that. The housing allows the cell to be pressurised, depressurised, and stored under pressure safely. The brass fittings for the housing allow the cell to be pressurised / depressurised, they can be removed so that the cell can be placed in its spinner, the spiral hose connects the cell to a conventional high pressure head / gas cylinder, and the extendable clamp allows the cell to be removed and placed in the cell safely, as well as placed in the NMR magnet.

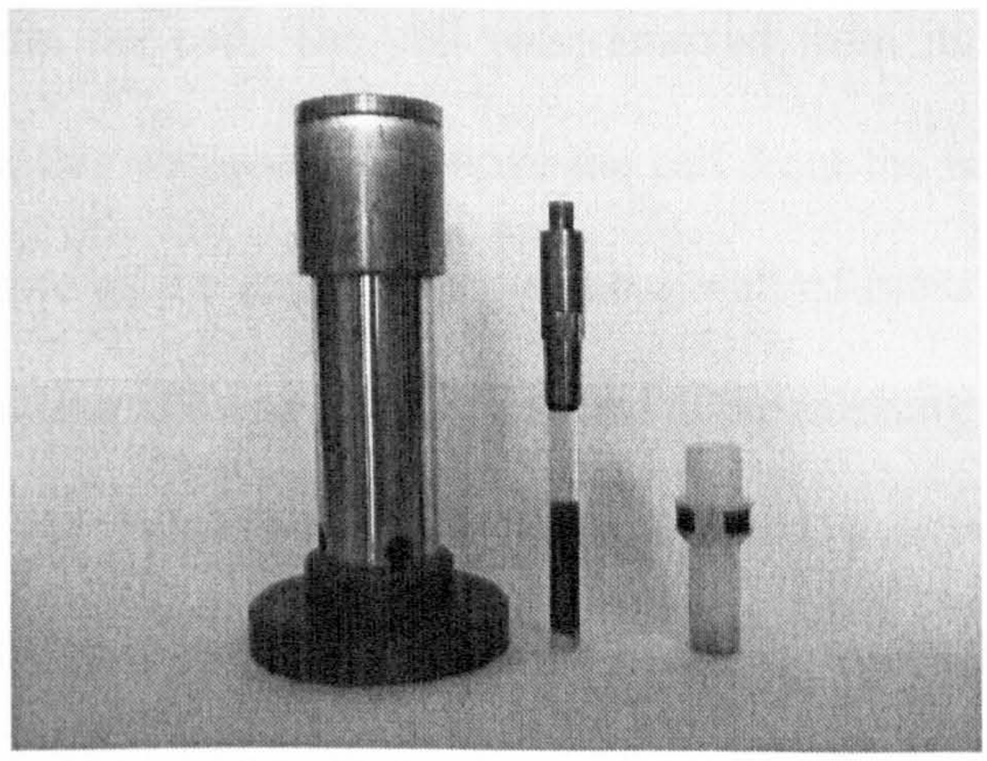


Figure 6- 2: ***Brass and aluminium NMR tube protective case, 10 mm high pressure NMR cell and spinner.***

Solutions containing the complex species to be studied were prepared as previously described in chapter 5. The solutions were prepared in d^4-methanol, or a mixture of d^4-methanol and d^2-dichloromethane. The high pressure NMR cell was degassed by removing the screw top and placing in a Shlenk tube, which was then degassed in the normal manner. The solutions containing the rhodium complexes were then transferred to the NMR cell under a stream of argon. The cell was then removed under an umbrella of argon and sealed by screwing on the screw top fully.

The cell was placed in the brass aluminium housing with a brass pressurising / depressurising attachment fitted. The spiral hose was attached to the cell via the screw top, and at the other end to a cylinder or autoclave containing the desired gas mixture. The hose was then degassed three times with the gas, the hose was left under a low pressure atmosphere of the desired gas mixture. The cell was then opened to the gas and pressurised to the desired pressure. The cell was left under pressure for 1 to 5 hours. The pressure in the hose was then released and the spiral hose detached from the cell. The cell was removed from its housing with the extendable clamp, this was used to remove the cell from the housing at all times when under pressure as the cell is kept behind a wall of brass within the clamp. The brass fitting which allowed pressurising and depressurising was then removed from the housing and replaced with the NMR spinner. The cell was then placed in the spinner with the clamp, and pushed down firmly to ensure the cell was tightly held in the spinner. The cell was then released from the clamp and was ready to be placed in the Bruker AM 300 NMR spectrometer.

The spin air and the gas uplift for the NMR spectrometer were turned off. The cell was removed from its housing with the extendable clamp. The bottom of the

clamp was fitted to the top of the NMR spectrometer. The cell was then lowered in the NMR magnet with the extendable clamp. The cell was then released from the clamp and the clamp removed from the spectrometer. The NMR spectrum of the solution was then acquired.

7.6. HPIR

The high pressure infrared autoclave consists of a Parr high pressure vessel with a single crystal silicon rod passing through it. The autoclave allows *in situ* pressure and temperature readings, catalyst injection and pressurising / depressurising through a tap. The autoclave is stirred mechanically from above. The silicon rod bathes in the reaction solution. The apparatus lies in the infrared beam with the laser beam focussed on the pointed end of the silicon rod which protrudes out of the vessel. The optics are optimised by making small adjustments to the autoclave position relative to the beam. The infrared spectrometer is set for ATR correction. Once optimised, the beam will pass into the rod, reflect along the inside of the crystal and pass out of the other end in to the infrared detector. At the surface of the rod the solution absorbs energy from the beam and the resultant beam which emerges is deficient in the specific frequencies absorbed by the species in solution. Heating is effected by heating rods which pass into holes in the base of the Parr vessel.

Solutions containing the complex species to be studied were prepared as previously described in chapter 5.

The autoclave was degassed by pressurising to 10 bar with argon or nitrogen, then releasing the pressure three times. Argon was then allowed to flow into the gassing / degassing side arm and out of the open injection port. The reaction

solution was then injected into the vessel through the injection port; substrate could be injected at this point in the same manner or later when the cell was at temperature and pressure by isolating the cell from the injection port before injecting the substrate. The autoclave was then sealed, pressurised to the required pressure with the required gas and tested for leaks. The autoclave was fixed into the infrared beam and the optics were optimised. The autoclave was heated to the required temperature. If required the substrate could be injected at this point by opening the valve between the injection port and the autoclave. To ensure that all the substrate was injected, the port was pressurised to a higher pressure than the autoclave. The FT IR spectrum of the solution could then be measured and saved to the hard disk of a PC. The background spectrum of the catalytic solutions under atmospheres of the same gases at identical pressures and temperatures had been previously taken in the same manner. Background spectra were then subtracted manually using the OMNIC package.

7.7. References

1. Clegg W., Eastham G.R., Elsegood M., Heaton B., Iggo J., Tooze R., Whyman R. and Zacchini S., *Organometallics*, **21** (2002), 1832

Chapter 8:

CRYSTAL STRUCTURES

8.1. [Rh(DTBPMB)Cl(CO)]

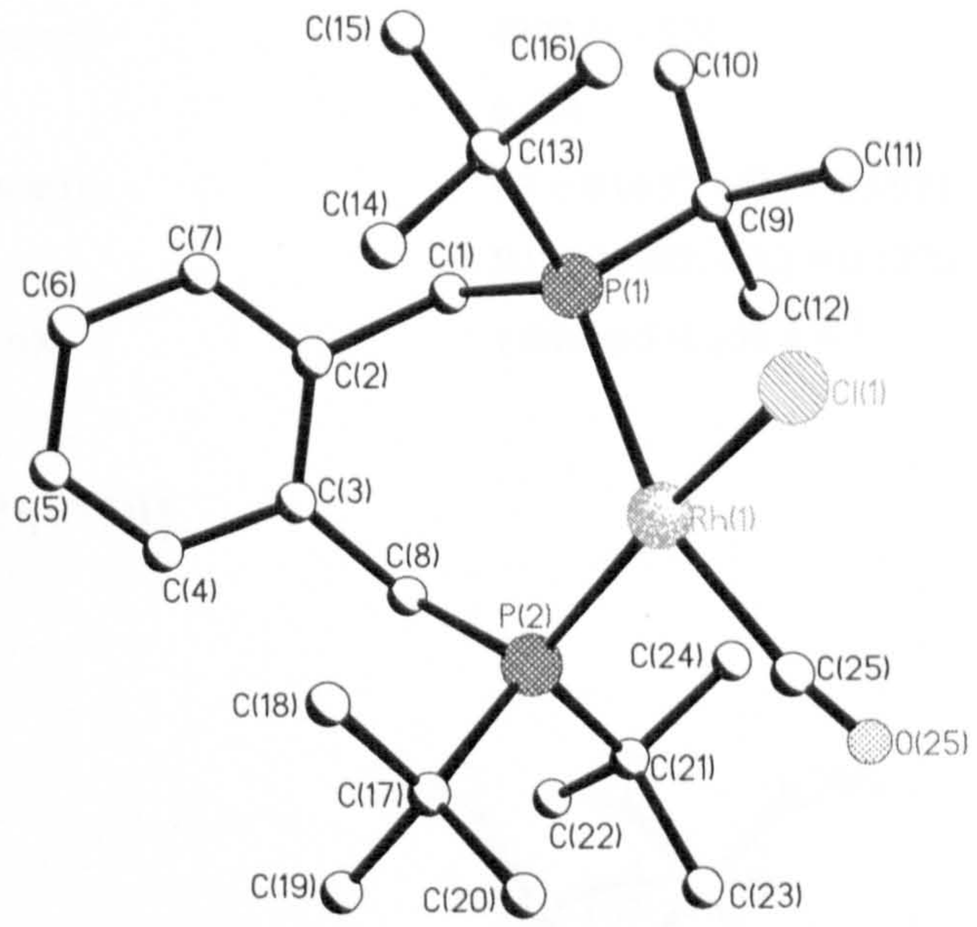


Table 1. Crystal data and structure refinement for cjdch5.

Identification code	cjdch5	
Empirical formula	C25 H44 Cl O P2 Rh	
Formula weight	560.90	
Temperature	125(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.476(3) Å	α= 77.071(7)°.
	b = 10.474(4) Å	β= 75.674(7)°.
	c = 16.257(6) Å	γ = 74.635(6)°.
Volume	1329.0(8) $Å^3$	
Z	2	
Density (calculated)	1.402 Mg/m^3	
Absorption coefficient	0.878 mm^{-1}	
F(000)	588	
Crystal size	.14 x .1 x .01 mm^3	
Theta range for data collection	2.62 to 25.53°.	
Index ranges	-9<=h<=10, -12<=k<=12, -18<=l<=19	
Reflections collected	8051	
Independent reflections	4797 [R(int) = 0.0682]	
Completeness to theta = 25.53°	96.4 %	

Absorption correction	multi-scan
Max. and min. transmission	1.00000 and 0.589335
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4797 / 0 / 271
Goodness-of-fit on F^2	0.764
Final R indices [I>2sigma(I)]	R1 = 0.0537, wR2 = 0.0971
R indices (all data)	R1 = 0.1202, wR2 = 0.1076
Largest diff. peak and hole	1.046 and -1.336 e.Å^{-3}

8.2. [Rh(DTBPMB)(CO)I]

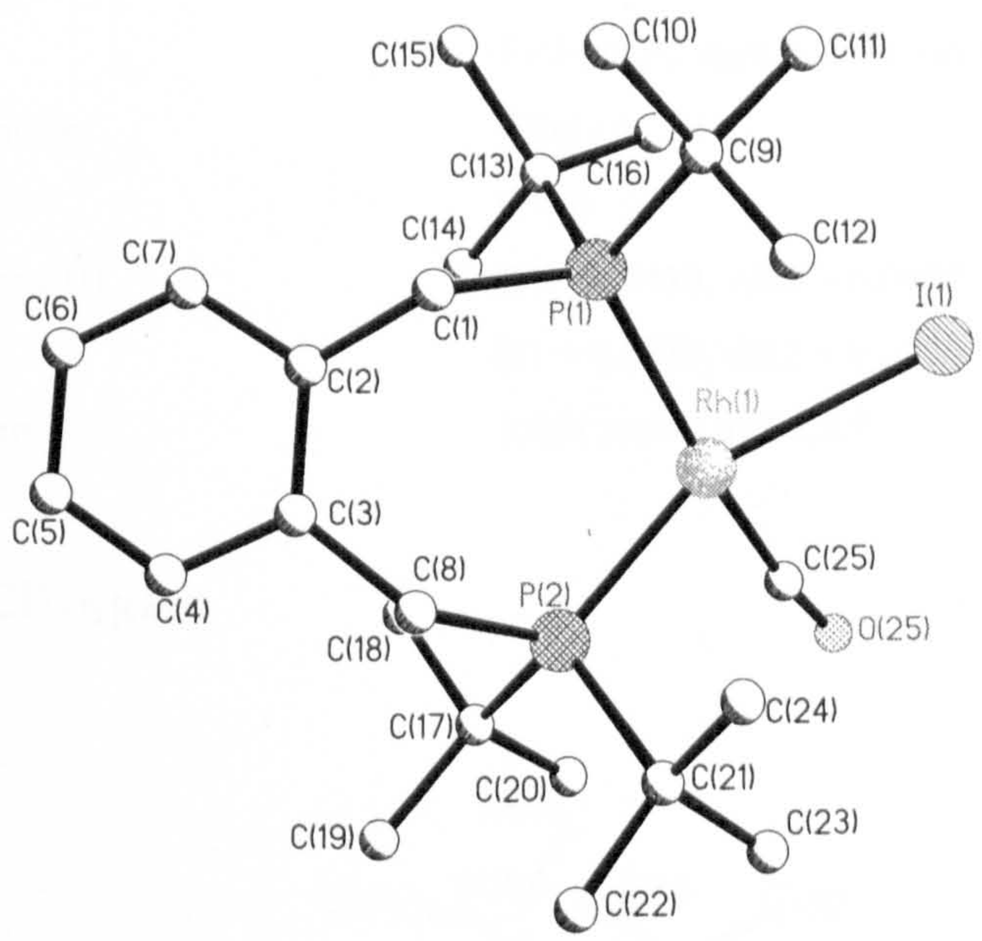


Table 1. Crystal data and structure refinement for cjdCh6.

Identification code	cjdch6	
Empirical formula	C25 H44 I O P2 Rh	
Formula weight	652.35	
Temperature	125(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 12.2158(12) Å	α= 102.122(2)°.
	b = 12.7064(13) Å	β= 106.790(2)°.
	c = 19.6855(19) Å	γ = 100.582(2)°.

Volume	2760.9(5) $Å^3$
Z	4
Density (calculated)	1.569 Mg/m^3
Absorption coefficient	1.867 mm^{-1}
F(000)	1320
Crystal size	.1 x .1 x .01 mm^3
Theta range for data collection	1.76 to 25.44°.
Index ranges	-14<=h<=11, -15<=k<=14, -23<=l<=23
Reflections collected	16256
Independent reflections	9905 [R(int) = 0.0340]
Completeness to theta = 25.44°	96.9 %
Absorption correction	multi-scan
Max. and min. transmission	1.00000 and 0.746379
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9905 / 0 / 541
Goodness-of-fit on F^2	0.966
Final R indices [I>2sigma(I)]	R1 = 0.0430, wR2 = 0.0997
R indices (all data)	R1 = 0.0619, wR2 = 0.1070
Largest diff. peak and hole	1.461 and -1.973 $e.Å^{-3}$

8.3. $[(DTBPMB)(CH_3)_2](I_3)_2$

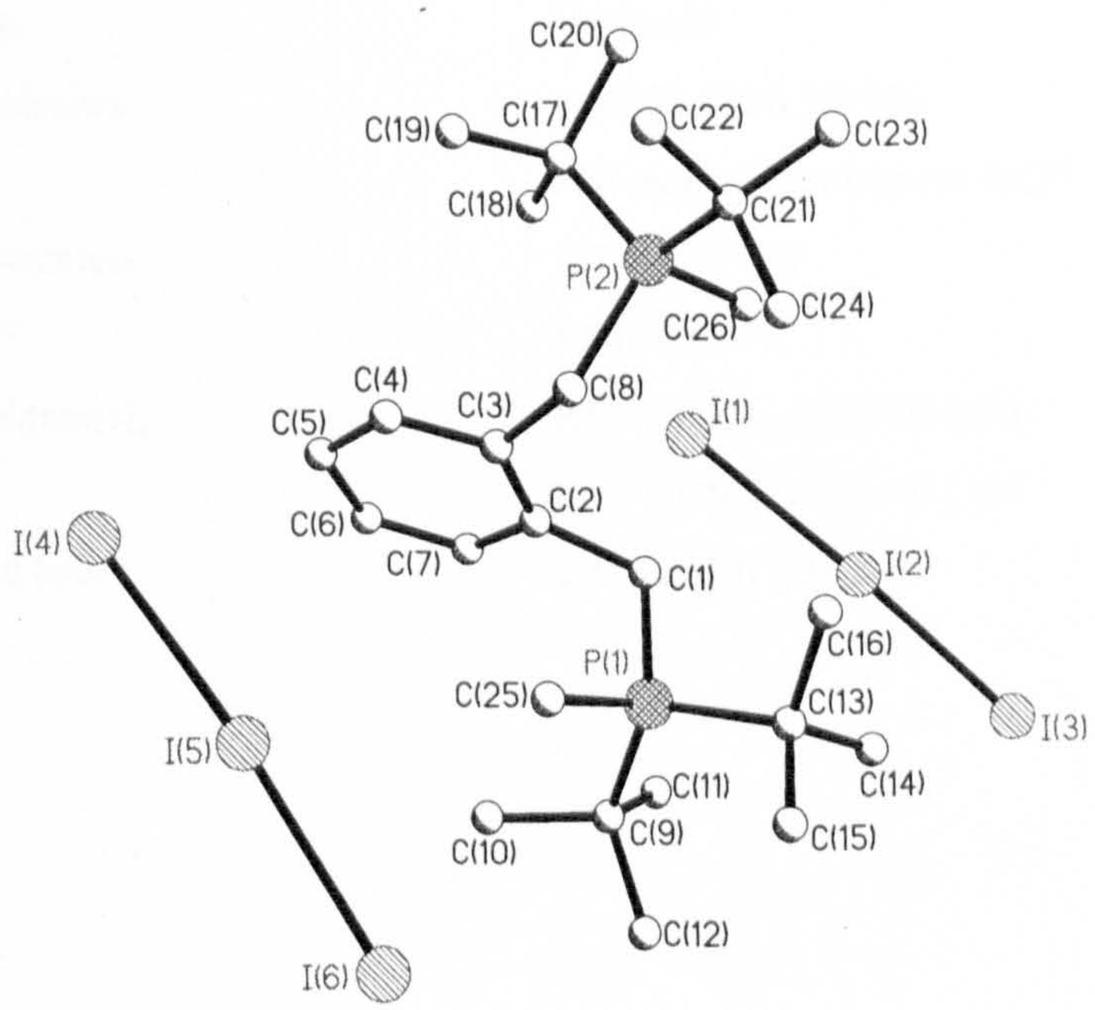


Table 1. Crystal data and structure refinement for cjdch7.

Identification code	cjdch7	
Empirical formula	C26 H50 I6 P2	
Formula weight	1186.00	
Temperature	125(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.9029(12) Å	α= 87.539(2)°.
	b = 11.3875(14) Å	β= 86.579(2)°.
	c = 34.978(4) Å	γ = 76.306(2)°.
Volume	3823.8(8) $Å^3$	
Z	4	
Density (calculated)	2.060 Mg/m^3	
Absorption coefficient	4.972 mm^{-1}	
F(000)	2216	
Crystal size	.1 x .1 x .03 mm^3	
Theta range for data collection	1.75 to 25.63°.	
Index ranges	-11<=h<=11, -13<=k<=13, -42<=l<=30	
Reflections collected	23048	
Independent reflections	13740 [R(int) = 0.0360]	
Completeness to theta = 25.63°	95.3 %	
Absorption correction	Multiscan	
Max. and min. transmission	1.00000 and 0.551918	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	13740 / 0 / 617	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0508, wR2 = 0.1058	
R indices (all data)	R1 = 0.0745, wR2 = 0.1135	
Largest diff. peak and hole	2.411 and -1.251 $e.Å^{-3}$	

8.4. $[Rh_2(DTBPMB)(Cl)_2(cod)_2]$

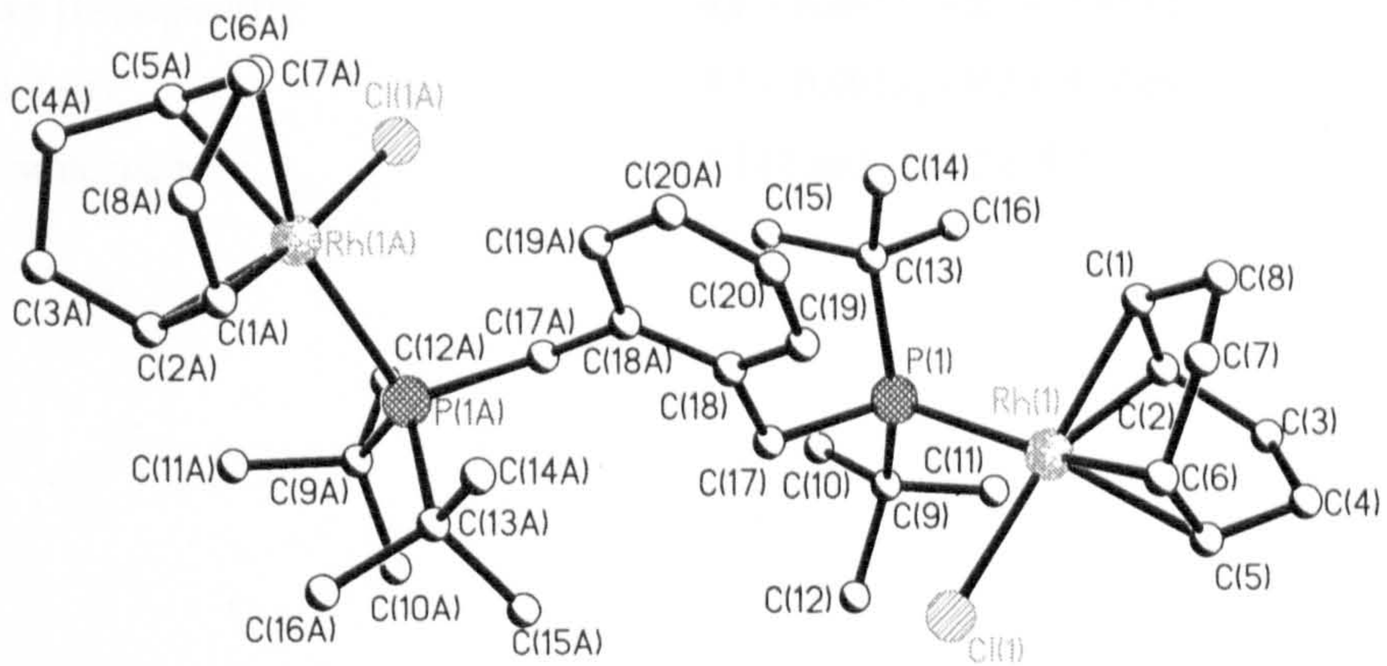


Table 1. Crystal data and structure refinement for CJDCH9.

Identification code	cjdch9	
Empirical formula	C40 H68 Cl2 P2 Rh2	
Formula weight	887.60	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 32.30(2) Å	α= 90°.
	b = 9.811(6) Å	β= 111.228(16)°.
	c = 14.041(10) Å	γ = 90°.
Volume	4148(5) $Å^3$	
Z	4	
Density (calculated)	1.421 Mg/m^3	
Absorption coefficient	1.028 mm^{-1}	
F(000)	1848	
Crystal size	0.1000 x 0.1000 x 0.0100 mm^3	
Theta range for data collection	2.18 to 25.35°.	
Index ranges	-38<=h<=31, -11<=k<=11, -11<=l<=16	
Reflections collected	11966	
Independent reflections	3729 [R(int) = 0.1008]	
Completeness to theta = 25.35°	98.0 %	
Absorption correction	Multiscan	
Max. and min. transmission	1.0000 and 0.4025	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3729 / 0 / 209
Goodness-of-fit on F^2	1.012
Final R indices [I>2sigma(I)]	R1 = 0.0671, wR2 = 0.1517
R indices (all data)	R1 = 0.0933, wR2 = 0.1669
Largest diff. peak and hole	2.142 and -1.002 e.$Å^{-3}$